New insights from children with early focal brain injury: Lessons to be learned from examining STEM-related skills

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Abstract

The study of cognitive development in children with early brain injury reveals crucial information about the developing brain and its plasticity. However, information on long-term outcomes of these children, especially in domains relevant to science, technology, engineering, and math (STEM) remains limited. In the current review, our goal is to address the existing research on cognitive development of children with pre- or perinatal focal brain lesion (PL) as it relates to children's STEM-related skills and suggest future work that could shed further light on the developmental trajectories of children with PL. We argue that examining STEM-related development in children with PL will have broader implications for our understanding of the nature of the plasticity children with PL exhibit as well as address theoretical questions in the field regarding the foundation skills for STEM, including visuo-spatial and mathematical skills.

Keywords: STEM, plasticity, brain, development, visuo-spatial, mathematical

The current issue marks the 50th anniversary of Developmental Psychobiology. During these 50 years, our understanding of the developing brain rapidly increased. Studies from diverse perspectives contributed to the increase. Animal studies provided powerful models of the developing brain, enabled causal examination of the role of environmental factors as well as how the developing brain responds to injury (e.g., Van Praag, Kempermann, & Gage, 2000). However, animal studies are limited in the range of cognitive skills they can shed light on. Brain imaging studies on typically-developing children (TD) revealed detailed information on the structural and functional neurocognitive basis of a wide range of cognitive skills and their development. These studies identified the neurocognitive networks that typically support cognitive skills. Yet, studies on TD children have not provided information on whether these networks are necessary and/or sufficient to support various cognitive skills (Levine, Raja Beharelle, Demir, & Small, 2015). In the current paper, we will review findings on the developing brain from another perspective; studies that are based on children with pre- or perinatal focal brain lesion (PL). We aim to summarize and discuss the existing literature on cognitive development of children with PL with a special focus on their cognitive skills that are related to science, technology, engineering, and math (STEM) – spatial and mathematical skills. Given the paucity of work in this area, our second goal is to highlight areas for future research and discuss the importance of a focus on STEM for our understanding of brain plasticity.

The study of children with PL presents a unique opportunity to examine the developing brain and enables researchers to examine reorganization and plasticity in the developing brain in response to a localized injury. These studies can reveal alternative networks that support favorable developmental trajectories as well as the possible limits of plasticity in the face of an early insult. Children with PL are a group of children who experienced focal brain lesions during or right after birth. Such injuries are relatively rare. The incidence rate is estimated to be around 1 in 4000 (Stiles, Reilly, Levine, Trauner, & Nass, 2012). These injuries are typically vascular injuries occurring during the third trimester, at birth or during the neonatal period. The nature of the resulting injury varies among children, ranging from lesions involving one hemisphere to those limited to a cortical or subcortical region. Most children with PL have normal to near-normal sensory and intellectual functioning (for further information about the mechanisms of PL, please see Stiles et al., 2012). Some types of PL, especially periventricular lesions, are frequently observed in preterm children. Because of other central nervous system (CNS) injuries and complicating factors in premature babies, the majority of the studies reviewed here include children with PL that are full-term (Krägeloh-Mann & Horber, 2007).

Children with PL and adults with brain injuries of similar nature differ in terms of their behavioral profiles (e.g., Bates & Dick, 2002; Stiles, Nass, Levine, Moses, & Reilly, 2009). Brain lesions that occur in adulthood are typically associated with significant, site-specific impairments. Similar lesions in children result in impairments to a lesser degree. The study of children with PL highlights a view of development as a dynamic process, where the developing brain adapts to factors at both neurological and environmental levels during development. Yet, many important questions regarding children with PL’s cognitive development remain unanswered. The majority of the extant studies focus on cognitive skills that develop in early years, such as language development. Less is known about children’s performance on complex domains that have implications for cognitive functioning later in life and eventual life outcomes. Specifically, to our knowledge, very limited work examined children’s cognitive performance related to STEM disciplines (e.g., Glenn et al., 2017; Murias et al., 2017; Stiles et al., 2005). How children’s skills related to STEM develop over time and how their developmental trajectories vary as a function of children’s biological and environmental characteristics remain unanswered.

Understanding skills related to STEM is significant because of practical reasons. Increasing numbers of jobs—not limited to professional scientists—require knowledge of STEM. STEM-related jobs are projected to increase by 17% from 2008 to 2018 compared to only a 9.8% estimated increase in non-STEM jobs (Langdon, McKittrick, Beede, Khan, & Doms, 2011). Indeed, National Assessment of Educational Progress report suggests that many students lack crucial STEM skills and as a result, are not well prepared for the demands of the future economy (NRC, 2011). Additionally, both individual and societal decisions increasingly require an understanding of STEM. Many daily activities, including making financial and medical decisions, and using different computer applications require STEM skills (Reyna, Nelson, Han, & Dieckmann, 2009). Therefore, it is crucial to increase STEM literacy for all children, including those who will not pursue a career in STEM disciplines.

Focusing on STEM skills is important for theoretical reasons as well. STEM performance is built upon cognitive skills that are established as early as infancy, but the developmental trajectory extends well into adulthood. Although the ability to use language flexibly and learn to read and write is almost invariant among adults (Paris, 2005), there is greater variability among individuals in terms of their STEM-related performance in adulthood (EU, 2016). Therefore, focusing on STEM performance is crucial to examine how early brain injury unfolds through development as children are faced with increasingly challenging cognitive tasks. In discussing skills relevant to STEM, our goal is also to examine the dynamically interacting factors that might contribute to the resilience of children with PL and contribute to favorable developmental trajectories. Specifically, we aim to leverage research on children with PL to better understand development as a dynamic process that unfolds in the context of interactions among factors at the neural, individual, and environmental levels of analyses. To fulfill our aims, we 1) briefly address existing research on children with PL's general cognitive skills that are related to STEM, 2) review emerging findings on children with PL's specific skills related to STEM, and 3) highlight areas open for research and importance of focusing on STEM development.

Building Blocks of STEM Performance

What are the general and specific skills that support STEM during childhood? We consider skills that are part-and-parcel to STEM performance as specific skills. These include visuo-spatial skills and mathematical skills (Shea, Lubinski & Benbow, 2001; Super & Bachrach, 1957; Uttal & Cohen, 2012). Recent research highlights the cross-domain interactions of STEM performance. Performance in STEM is also reliant upon on a wider range of cognitive skills. We consider a broader set of cognitive skills, including overall intellectual performance, executive function, language, and literacy skills, as general skills supporting STEM performance (Blums, Belsky, Grimm and Chen, 2016). We acknowledge that STEM performance is a broad construct and encompasses multiple disciplines ranging from computer programming to biology to architecture. Here, we primarily focus on skills that are relevant to STEM in earlier years- the building blocks of STEM. For ease of reading, however, we refer to these STEM-performance relevant skills as STEM skills in the reminder of the paper.

Before we go further, we would like to highlight that this is not an exhaustive literature review of children with PL's cognitive development. Excellent reviews of children with PL's development in a diverse set of cognitive domains have been presented elsewhere (Bates & Dick, 2002; Levine et al., 2015 Stiles et al., 2012). In addition, the current review specifically focuses on children who experienced unilateral, focal, and pre- or perinatal injury. Thus, we exclude children with traumatic brain injury, preterm children, children with low birth weight, children with bilateral lesions, and children with lesions that occurred later in life. At a workshop sponsored by the National Institute of Child Health and Human Development and the National Institute of Neurological Disorders and Stroke of the National Institutes of Health of the United States (Raju et al., 2007), perinatal stroke was defined as occurring between the 20th week of gestation and the 28th postnatal day. We adhere to this definition and in doing so, we are able to discuss brain plasticity in the face of an early, localized injury and without other complicating factors. However, because limited work examined development in STEM domains, we also include some findings from children with *early* brain injury- defined as stroke during the first year of life and mention this in the relevant section. Additionally, we discuss findings on children with lesions occurring later in life only when these children are included as a comparison group to children with PL or when there are no other studies on children with PL in a given domain.

General Cognitive Skills Supporting STEM: Intellectual Functioning, Executive Functions, and Language-literacy Skills

In this first section, we will briefly review existing studies in overall intellectual, academic functioning, and language-literacy skills of children with PL. For the purposes of the current paper, our goal is to identify common themes, and discuss the possible relevance of development in these domains for STEM performance.

Overall intellectual functioning

Overall intellectual functioning is one of the most well studied aspects in children with PL. The existing literature primarily depends on standardized tests of IQ. Relations between general intelligence and STEM have been reported both at the individual and the macro-societal level

(Deary, Strand, Smith & Fernandes, 2007; Rindermann, 2007). Nevertheless, the relations between assessment of IQ and performance on STEM-related tasks remain difficult to interpret. The similarities could be due to a multitude of factors, including similarities of the items included in IQ and STEM-relevant tests or the cognitive demands required by these tests (Rindermann, 2007). For example, some of the spatial skills central to STEM, such as visualization, is a component skill of IQ (Newcombe & Frick, 2010).

Many common themes emerge across the studies on IQ. Lower performance on IQ tests by children with PL compared to typical children has been reported in a variety of studies (e.g. Ballantyne et al., 2008; Levine et al., 2005; Westmacott, MacGregor, Askalan, & deVeber ,2010). However, more significantly, a common theme across different studies is the heterogeneity in performance across children with PL. In explaining the heterogeneity, lesion site or laterality do not associate with specific deficits. Westmacott et al., 2010 investigated intellectual ability in children with PL who experienced arterial ischaemic stroke (experienced during the prenatal period or within the first 28 days of the postnatal period). Children with PL were on average 8 years old at time of testing. The children with PL group performed poorly compared to the normative TD sample on multiple measures of IQ (e.g. full-scale, performance, verbal). Importantly, lesion location or laterality did not predict IQ scores. In terms of lesion laterality, although some studies report lesion laterality effects in certain subtests, the majority of the literature has not reported significant hemispheric differences (Aram & Ekelman, 1996; Ballantyne, Scarvie and Trauner, 1994; Ballantyne et al., 2008; Goodman & Yude, 1996; Westmacott et al., 2010). Lesion size, on the other hand, is proposed to have significant consequences for children’s intellectual functioning (Levine et al., 2005). It should be noted that size and type of the lesions are related, deeming it hard to pinpoint the role of lesion size versus type. For instance, periventricular lesions that result from hemorrhages affect white matter tracts in the brain, occur mainly in the early third trimester of pregnancy, and tend to be smaller in size. Vascular lesions that result from ischemic infarctions, on the other hand, affect gray mater structures, occur during late third trimester or during birth, and tend to be larger in size (Krägeloh -Mann, 2004).

Other studies focusing on cognitive functioning include a wider range of measures, such as working memory. One of the most consistent predictors of general cognitive functioning is the presence of epileptic seizures that exist beyond the neonatal period (Ballantyne, Spilkin, Hesselink, and Trauner, 2008; Kolk et al., 2011). Specifically, cumulative effects of seizures may hinder ongoing learning. In a longitudinal study, Ballantyne, Spilkin, Hesselink, and Trauner (2008) reported a decrease in full scale IQ of children with PL compared to controls. Further, within the children with PL, children who experienced seizures over time had lower scores compared to the children without seizures. The non-seizure group consistently performed better than the seizure group on IQ measurements as well as other specific cognitive processes, such as attention and memory. Longitudinally, both the non-seizure and control groups showed a small but significant increase in their IQ development over time, while seizure group did not. Therefore, the presence of seizures might limit the degree of plasticity after PL.

The studies mentioned above highlight the importance of examining developmental trajectories of children with PL. Indeed, studies find that some of differences between typically developing (TD) children and children with PL in terms of cognitive and IQ measures might increase with age, such as the fall-off in IQ described above (Banich, Levine, Kim, & Huttenlocher, 1990; Buuren et al., 2013; Levine, Kraus, Alexander, Suriyakham, & Huttenlocher, 2005; Westmacott, MacGregor, Askalan, & deVeber, 2010). Some investigations suggest that the fall-off over time might be greater for children who have smaller lesions and show milder deficits earlier in life (Levine et al., 2005). There are two possible views in explaining why cognitive difficulties increase at later ages. Anderson, Spencer-Smith and Wood (2011) hypothesized that children with brain injury (including children with PL) may “grow into” their deficiencies. The plasticity of the brain might compensate early in development. With increasing demands of more complex processes, however, it might be no longer possible that this compensation could overcome the deficiencies. Another explanation is that children showing no delays at preschool years may manifest these deficits at school years due to the more proficient requirements of those ages developmentally. A group difference that is not apparent on less-demanding tasks appropriate for younger kids might emerge on more-demanding tasks administered to older children.

Executive functioning

Executive functioning (EF) refers to top-down mental processes that are involved in controlling, planning, and monitoring thoughts, emotions, and actions (Diamond, 2013). EF requires abilities such as selecting proper information while preserving it in addition to making and modifying judgments. Miyake et al. (2000) postulated three core components of EF - shifting (cognitive flexibility), updating (working memory), and inhibition (suppression of prepotent responses). These processes are crucial for the integration of external stimuli, goal-planning, and strategy formation as well as taking initiative for proper action (Luria, 1973).

Executive functioning projects to several aspects of everyday life, including decision making (MacPherson, Phillips, Della Sala, 2002) and emotion regulation (Zelazo & Cunningham, 2007). EF is also closely related to both language and literacy skills and, more importantly for our purposes, to mathematical (Blair & Razza, 2007; Bull, Espy, & Wiebe, 2008; Bull & Scherif, 2001; Clark, Pritchard & Woodward, 2010; Clair-Thompson & Gathercole, 2006; Hackman, Gallop, Evans, & Farah, 2015) and visuo-spatial skills (Miyake, Friedman, Rettinger, Shah & Hegarty, 2001). Three core components of EF have close relationships with a variety of STEM-related activities. For instance, working memory is needed to solve simple mathematical problems because they require both preserving the information and manipulating it. Likewise, complex science texts cannot be comprehended unless relevant information is filtered, and irrelevant information is inhibited. Adapting to the changing demands of school tasks requires cognitive flexibility as well. Thus, EF plays a key role in STEM performance (McClure, Guernsey, Clements, Bales, Nichols, Kendall-Taylor, & Levine, 2017).

Only a handful of studies examined EF development in children with brain injury, and to our knowledge one in children with PL (Jacobs, Harvey, & Anderson, 2011). In this particular study, the sample included children with pre- and postnatal lesions and the results were presented for the combined group. Given the paucity of studies in this domain, we present the results for the combined group. 79 children with focal brain injury (aged 7 to 16) were compared with typically developing controls on various aspects of cognitive abilities including attentional control, goal setting, cognitive flexibility as well as motor time performance. Children with focal brain injury performed significantly worse in all cognitive and executive functioning tasks compared to controls, regardless of lesion site. Other work with children who suffered stroke beyond the perinatal stage suggests that the timing, as opposed to the location, of the lesion might be the more determinant factor for executive functioning abilities (Max, Bruce, Keatley, & Delis, 2010). Following the age effects on children with PL's performance discussed above, we note that because EF has an extended developmental trajectory extending into adolescence, it might be more vulnerable to disruption by later stroke (Blakemore & Choudhury. 2006; Carlson, 2005;

Carlson & Moses, 2001; Zelazo et al., 2003). In sum, limited research suggests that EF skills of children with brain injury might be worse than TD children. Yet, future work is needed to specifically focus on the effects of prenatal injury.

Language development

In TD children, language development goes through relatively predictable stages. Children start communicating through gestures around 9 months, comprehend their first words as early as 6 months of age, produce their first words around 12 to 18 months, and combine words into sentences before 24 months. Between the 2nd to 4th year of life, the complexity of children's syntax rapidly increases, and by age 4, children have a basic command of the syntax of their language. Starting around age 4, children learn to use language for a diverse set of functions such as telling stories and making inferences (e.g., Hoff, 2013; Parish-Morris, Hirsh-Pasek, & Golinkoff, 2013). At every stage, however, children also vary greatly from each other in their language skills.

Early language ability has strong ties to STEM achievement (Duncan et al., 2007; Hooper, Roberts, Sideris, Burchinal, & Zeisel, 2010). Performance in the four Language-Arts strands identified in the Common Core state standards (reading, writing, speaking, and listening) are considered crucial for STEM learning and STEM provides a context where all components can be practiced together (McClure et al., 2017). Ties between language and STEM skills are identified even before school entrance. For example, the language input children receive from their parents during block play in preschool years predicts higher spatial skills when children reach school entrance (Pruden, Levine, & Huttenlocher, 2011). Another study establishing long-term relations showed links between language competence (reading decoding and vocabulary) at 54 months and STEM achievement at 9th grade (GPA in math and science classes) (Blums, Belsky, Grimm, and Chen, 2016). Highlighting the importance of language skills for success in STEM, prior work on English-language learners show that they experience disproportionate difficulty in mathematical (Martiniello, 2008) and science domains (Lee, 2005). Later-developing language skills, including knowledge of rare words, complex syntax processing, and narrative comprehension are similarly crucial for STEM performance. The formal academic language of science and math texts requires understanding rare words and syntactically complex sentences, such as those with passive voice and inference making skills to evaluate the claims of these connected texts (Snow, 2010). Gesture is highlighted as a central tool in STEM domains too (Stieff, Lira, & Scopelitis, 2016).

The majority of the studies in children with PL focused on their earlier developing language skills (for a detailed review, see Levine et al., 2015). Overall, children with PL show initial delays when getting their language off the ground. For instance, children with PL are initially delayed compared to their TD peers in their babbling, early gestures, vocabulary, and syntactic development (Bates & Roe, 2001; Bates et al., 1997; Demir et al., 2010; Feldman, 2005; Trauner et al., 2013). By the beginning of school years, children with PL seem to catch up and perform within the low-normal to normal range in terms of their earlier developing language skills (Stiles et al., 2012). The nature of language development in children with PL is similar to that of TD children. In TD children, speech and gesture couple tightly - gesture precedes and predicts many milestones in TD children's language development. For example, TD children point to an object before the word for the same object enters their vocabulary (Iverson & Goldin-Meadow, 2005). Although children with PL experience initial delays in their language development, the tight relation observed between speech and gesture remains intact in children with PL's language development. A study by Sauer and colleagues (2010) showed that, as for TD children, early gesture production predicts vocabulary size in children with PL. Children with PL whose gesture production was low (below 25th percentile) at 14 months of age had smaller vocabularies 1 year later compared to children with PL whose gesture production was higher (above 25th percentile). Gesture leads the way for simple syntactic sentences as well. Both TD children and children with PL produce simple sentences across gesture and speech (e.g., ‘cookie’ + eat gesture) before they can produce such constructions in speech alone (e.g., ‘eat cookie’). However, as opposed to simple sentences that are produced across speech *and* gesture first, children with PL express complex sentences (e.g. ‘I want dad to wind it up’) first *only* in speech. Importantly, these complex constructions produced in speech are delayed in children with PL compared to TD children. A possible explanation is the increased motoric demands of such constructions making it harder for children with PL to express them via gesture, which in turn might have delayed their production in speech (Özçalışkan, Levine, & Goldin-Meadow, 2013). Overall, as in TD children, gesture serves as a harbinger of linguistic change in children with PL.

The plasticity children with PL reveal for earlier developing language skills seems to exhibit a possible limit when children are faced with more complex language tasks in school years. For instance, around 5-6 years old, an age when children with PL do not differ from their peers on vocabulary or syntax tasks, their narrative production skills lag behind (Demir et al., 2010; Reilly, Wasserman, & Applebaum, 2013). Similarly, children with PL underperform when their language planning or online language processing skills, especially of complex syntactic structures, are assessed (Dick et al., 2004; MacWhinney et al., 2000). Studies that follow children with PL into their late school years remain limited. Thus, whether difficulties on complex tasks represent true limits to plasticity or whether children with PL will catch up to their peers remain as open questions.

Mirroring the findings on cognitive development, in the domain of language development, certain lesion characteristics explain children's performance better than others. Lesion site and size do not predict children's language performance in the same way as they do for adults with focal lesions (Chilosi et al, 2001; Reilly et al., 2008). Even in the studies that report lesion site differences, the effects could be attributed to the associations to lesion size (Bates et al., 1997). Lesion size and type tend to be correlated that makes it harder to pinpoint the role of a single lesion characteristic. Children with larger lesions and vascular lesions lag behind compared to their peers. One study following children with PL between 14 and 46 months of age reported that children with vascular lesions have smaller vocabularies and shorter utterances than children with periventricular lesions, whereas children with periventricular lesions do not differ from their TD peers (Rowe et al., 2009). Taken together, research shows that even though children with PL exhibit some early delays in language development, they catch up by the school years. However, some language skills, such as language processing or narrative production, can be worse for children with PL compared to TD children. Children with PL vary in their language performance and lesion characteristics predict these differences.

Reading development

Successful reading requires two component skills: decoding and comprehension (Hoover & Gough, 1990). Decoding refers to the bottom-up identification of printed words by mapping orthographic representations to phonological representations, and then accessing the entry of the phonological form in the mental lexicon. Reading comprehension refers to the processing of the lexical information from the orthographic representation of the text, deriving sentence and discourse interpretations, making inferences, and linking the information in the text to background knowledge. Typically, most children become proficient at decoding the written language around 3rd grade and consequently start better comprehending what they decode (e.g., Roth, Speece, Cooper, 2002). This transition is also referred to as transitioning from learning to read to reading to learn.

Strong reading skills are crucial for academic success, including success in STEM disciplines (Cromley, Snyder-Hogan, & Luciw-Dubas, 2010). As discussed above, Blums, Belsky, Grimm, and Chen (2016) showed links between reading decoding at 54 months and STEM achievement at 9th grade (GPA in math and science classes). Similarly, significant correlations were found between 15-year-old students' scientific literacy and reading literacy on the Programme on International Student Assessment (PISA) (Cromley, 2009). More specifically, reading and mathematics share similarities in that both are recent historical inventions and depend on the ability to process symbols (Dehaene & Cohen, 2007).

Only a few studies compared reading development of children with PL to their TD peers. The existing findings overall seem to mirror the language development literature. Children with PL as a group significantly fall behind their peers in their reading development, but do not exhibit significant difficulties exhibited by adults with similar injuries (Aram & Ekelman, 1988; Ballantyne, Spilkin, Hesselink, & Trauner, 2008; Frith & Vargha-Khadem, 2001). One study by Demir-Lira and Levine (2016) comparing reading development trajectories of TD children and children with PL between Kindergarten and 2nd grade showed that as a group, children with PL were delayed in their reading decoding and comprehensions skills, but their performance was within the normal range compared to TD children. Group differences were primarily due to children with larger lesions and children with right hemisphere damage underperforming compared to their peers (Demir-Lira & Levine, 2016). This study also compared growth during the school year versus summer months. Children with right hemisphere (RH) lesions exhibited greater growth during the school year and shallower growth during summer months compared to TD children and children with left hemisphere (LH) lesions. Findings suggest that school input might play an important role for children with PL who are at the highest risk for reading difficulties. The results on children with RH lesions should be considered with caution however because the sample of children with RH lesions was small. Other studies showed children with LH lesions underperforming (Frith & Vargha-Khadem, 2001) or reported no lesion side effects in reading (Ballantyne et al., 2008). Although further studies are needed to examine children with PL's school performance, existing studies demonstrate that examining learning trajectories of children with PL might reveal additional information to focusing on measurements from a single time point.

Summary

The studies reviewed above reveal important lessons about children with PL specifically and the developing brain more generally. The first important point is the great heterogeneity across children with PL's development. Although general group trends can be identified, biological characteristics of children's lesions strongly predict their outcomes. The studies differ in the lesion characteristics they explore, but across different studies, lesion size and type seem to play a more important role than lesion laterality and site in predicting children's performance. Another take-home point from the studies discussed above is the importance of studying developmental trajectories rather than isolated points in time. Two children might perform the same on a standardized test, but the trajectories they took to come to that point might differ from each other. The existing studies also suggest that children with PL might exhibit a delay/catch-up profile for each emerging cognitive skill. Existing work shows that children might exhibit specific difficulties for later-developing, complex cognitive skills. Given the limited number of longitudinal years in later year, whether a similar delay/catch-up will be observed for these skills remain unknown. Overall, the studies of children with PL highlight a view of development as a dynamic process, where the developing brain adapts to factors at the both neurological and environmental level. Finally, although performance in the areas cited above have been shown to play a crucial role in TD children's STEM development, to our knowledge, not much is known about how they relate to STEM performance of children with PL.

Specific Skills Related to STEM: Spatial and Mathematical Skills

We now turn our attention to skills that are part and parcel to STEM - spatial skills and mathematical skills. As research in technology and engineering in childhood is only recently developing and very limited, we exclude these areas from the current review.

Spatial skills

Spatial skills, as a fundamental aspect of human cognition, encompass understanding the relations within and between objects (e.g., shapes, locations), transforming these relations (e.g., mental rotation), and navigating in space. Spatial abilities of individuals are related to both choosing STEM careers and success in these disciplines (Wai et al., 2009). Spatial skills have even been considered as a gateway or barrier to STEM disciplines (Uttal & Cohen, 2012). Importantly spatial skills are malleable (Uttal et al., 2013), thus interventions can have an impact on both improving spatial reasoning and as a result success in STEM disciplines (Newcombe et al., 2013). Likewise, when we detect any problems related to spatial reasoning in children with PL, those deficits may be ameliorated with training.

Newcombe and colleagues (2013) divide spatial development into two components: the development of intrinsic spatial representations and extrinsic spatial representations. The former representations refer to understanding the properties of objects and manipulating them such as in mental transformations or rotations of objects. The latter representations are related to how an individual navigates in space. There is considerable research on both domains with TD children (for reviews see Newcombe et al., 2013; Newcombe & Frick, 2010; Vasilyeva & Lourenco, 2012). Very few studies have examined the effects of early brain injury on the development of intrinsic and extrinsic spatial representations (e.g., Murias et al., 2017; Stiles, Nass, Levine, Moses, & Reilly, 2009). Spatial skills of children with PL have mostly been investigated regarding the visuospatial skills and spatial grouping (e.g., Askhoomoff, Feroleto, Doyle, & Stiles, 2002; Schatz, Ballantyne, & Trauner; 2000; Stiles, 1998; Stiles, Stern, Trauner, & Nass, 1996; Stiles, Bates, Thal, Trauner, & Reilly, 2002).

Visuospatial skills. Visuospatial processing such as object unity, form perception, and complex pattern perception is present in infancy for TD children (e.g., Cohen, Chaput, & Cashon, 2002). Visuospatial processing involves two levels: global and local level of processing. Global level processing is the perception of overall configuration and involves the right hemisphere to a greater extent than the left. In contrast, local level processing is attending to the details of a visual scene and involves the left hemipshere to a greater extent than the right (Delis, Kiefner, & Fridlund, 1988). Many studies show that compared to TD children, children with PL can have impairments at both the global and local level of visuo-spatial processing. For instance, children with LH lesions have problems in processing local level elements and details of a scene whereas children with RH lesions show greater impairment in global level processing and spatial integration (Askoomoff et al., 2002; Schatz, Ballantyne, &Trauner, 2000; Stiles, Stern, Trauner, & Nass, 1996; Stiles, Trauner, Engel, & Nass, 1997). Drawings of children with RH lesions also lack coherence (Stiles-Davis, Janowsky, Engel, & Nass, 1988).

PL can impact children's spatial grouping too. In one study that included children with PL and children who had brain injury in the first 7 months of life, when asked to play freely with blocks, children with left and right hemisphere lesions differ how they spatially group the blocks. Preschool aged children with LH lesions have impaired local relations within the spatial array and children with RH lesions have problems putting blocks into a coherent spatial grouping. These match with their problems in overall visual processing. By age 4, children with LH lesions catch up their TD peers (Stiles et al., 1996; see also Stiles & Nass, 1991). Yet, the *process* of constructing the complex blocks is still different than TD children; children with left hemisphere lesions use simpler processes such as stacking or putting blocks in a line as opposed to placing a combination of blocks in more than one direction (Stiles et al., 1996).

Overall, the impairments that children with PL have in spatial tasks parallel adult profiles with similar injuries. Yet, deficits displayed by children are milder than the ones found in adults, and children can better compensate for their impairments (Stiles, Nass, Levine, Moses, & Reilly, 2009). Even though the deficits on visuospatial processing in both groups improve significantly by age, the pattern of problems continues, as subtle specific patterns of impairments can be apparent throughout development (Stiles, Reilly, Paul, & Moses, 2005). These skills are particularly related to processing objects and combining different parts to form a unified whole. Thus, these skills are necessary for intrinsic spatial representations. Nevertheless, for success in STEM related skills, children should be able to mentally rotate and transform these objects, which go beyond the spatial skills examined in children with PL.

Spatial location. Studies with adults and TD children demonstrate that the left hemisphere is involved more in coding categorical spatial relations (e.g., over, below), and the right hemisphere is involved more in encoding coordinate spatial relations that describe the precise metric information of the distance between objects or locations of objects (e.g., 100 meters away from each other) (Kosslyn, Thompson, Gitelman, & Alpert, 1998; Laeng, Chabris, & Kosslyn, 2003). The representation of spatial locations is one of the key aspects of extrinsic spatial relations. TD toddlers encode spatial location of an object hidden in a large sandbox by using distance information. Children both represent the exact location of the target object and incorporate information related to the larger spatial scale where the target object is located. Although young children accurately find where the object is hidden, their responses are biased toward the center of the space (Huttenlocher, Newcombe, & Sandberg, 1994). Moreover, 3- to 5-year-old TD children demonstrate a different category bias: they split the space into two categories and each half has its own prototypical center (Huttenlocher & Lourenco, 2007). Three- to 5-year-old children with left PL are very accurate in finding a hidden object; yet, they present category effects like 16- to 24-month-old TD children (i.e., having one category bias toward the center). Three- to 4-year-old children with right PL were less accurate in their performance compared to children with left PL. By 5 years of age, children with right PL also perform like children with left PL. However, the groups do not display category effects of their age matched typically developing peers (see Reilly, Levine, Nass, & Stiles, 2008). Overall, the performance of the children with PL is similar to TD children, but the process by which children reach their performance might vary from TD peers.

Spatial navigation. Extrinsic skills like spatial navigation have not been studied extensively in this population. One recent study by Murias and colleagues (2017) showed that children with PL perform similarly to TD children on a video game that tests their spatial navigational abilities. They conclude that cognitive skills that rely on distributed networks can be less vulnerable to early injury and can be more resilient (Kolb et al., 2011). Nevertheless, it is difficult to directly compare the results of this study with other spatial studies mentioned above, as children in this study were older than preschool age (i.e., aged between 6 and 16).

In sum, although children with PL have early deficits in visuospatial tasks and spatial location tasks, they catch up to their TD peers, particularly for accuracy measures. The time course of spatial processing may be different than TD children (Reilly, Levine, Nass, & Stiles, 2008). Nevertheless, several questions remain unanswered regarding children with PL's spatial reasoning. First, further studies are essential to examine prenatal brain injuries' effects on different spatial skills (i.e., intrinsic and extrinsic spatial skills). Future work is particularly crucial to assess whether all spatial skills go through similar trajectories. Second, studies show that in typical development spatial skills are flexible and can be improved by training (Uttal et al., 2013). Is it also true for children with PL? Third, research with TD children suggest that parents' use of spatial terms increase children's spatial skills (Pruden et al., 2017). How spatial input would mediate the link between PL children's possible problems in early spatial skills and later spatial reasoning is also an open question. Longitudinal studies are needed to assess this link. All these new lines of research can enhance our knowledge on the plasticity of spatial reasoning.

Mathematical skills

To our knowledge, very little is known about mathematical abilities of children with PL. Even less information is available about the roots of mathematical competency that develop in preschool years. A recent review on cognitive outcomes of children with PL did not report a single study on these children's math performance (Murias et al., 2014). Math skills and their earlier building blocks are at the core of STEM performance and education. For example, strong mathematical skills during adolescence predict entrance into STEM disciplines and further strong STEM achievements (Lubinski & Benbow, 2006; Wai et al., 2009). Mathematics achievement in school is predicted by children's early numerical knowledge (Siegler et al., 2012). Indeed, math-related skills at school entry are particularly strong predictors of academic performance in later grades, compared to reading or attention skills (Duncan et al., 2007). Children's arithmetic skills are built upon earlier developing precursor numerical skills. Here, we will first review two groups of such skills: children's symbolic skills and non-symbolic skills.

Symbolic number knowledge. An important precursor of later school math performance is verbal or symbolic number knowledge. This knowledge consists of verbal subitizing (ability to name small collections without counting), counting and understanding counting principles (e.g., 1-1 correspondence, stable-order), numerical magnitude comparison, linear representations of number (understanding that numerical magnitude linearly), and arithmetic operations. Children start using count words to label small quantities around the time they learn to talk or recite the count list soon after, but they might not know what these words mean. Principles of counting are not established until Kindergarten (Sarnecka, 2015). Around 4 years of age, children are able to discriminate between quantities and solve simple arithmetic problems. Children's understanding of linear representations of number extends into 2nd grade (Jordan & Levine, 2009).

Only a handful of studies examined children with PL's symbolic number knowledge. A recent study by Glenn and colleagues (2017) examined symbolic numerical knowledge of 4- to six-year-old children with PL and TD peers using a test of cardinal number knowledge and a standardized test of numerical ability, the Test of Mathematical Ability (TEMA-3). Cardinal number knowledge was assessed using the Point-to-X task (Wynn, 1992), in which children are presented with a single image that has two sets of squares, and are asked to point to the set that represents the number "X." Results showed that children with PL might experience a slight delay in getting their symbolic number skills of the ground, but they do not suffer from significant difficulties or site-specific difficulties adults with similar injury typically suffer from. However, children with cerebral infarcts and children with seizures performed lower than their peers with PL and their TD peers. In a study of two cases with perinatal lesion (one with LH, one with RH), children were administered a standardized test of arithmetic processing in school years. Both of the children performed within 1 standard deviation of the typical mean on this test (Stiles et al., 2003).

An earlier study included 7- to 22-years-old children with brain injury, but children varied in the timing of their brain lesions, ranging from lesions at birth to lesions at 15 years of age (Ashcraft, Yamashita, & Aram, 1992). Participants were administered the Number System, Computation and Applications subtests of the Stanford Diagnostic Mathematics Test and a battery of tests assessing different aspects of numerical cognition. Overall, children fell behind their TD peers on a range of tasks, specifically more difficult ones, such as complex verbal counting or speeded addition. The group differences were more pronounced for individuals with LH lesions. Unfortunately, children with PL's performance was not analyzed separately from children whose lesion onset was later in life, but correlational analyses showed a negative relation between performance and age of lesion onset. Given the paucity of studies in this area and the heterogeneity in the characteristics of the included children, many questions remain unanswered in mathematical cognition.

Non-symbolic number knowledge. The roots of mathematical performance could be traced back to even earlier years, as early as infancy. The ability to process numerical magnitudes in non-symbolic formats (such as dots) is considered a possible precursor to children's later performance on mathematical tasks (Mazzocco, Feigenson, & Halberda, 2011). Non-symbolic magnitude comparison tasks, such as dot comparison tasks, are used to assess non-symbolic numerical capacities. The capacity is present in preverbal infants but becomes more finely tuned with age. The system that allows approximate representation of numbers, is referred to as the approximate number system (ANS) (Dehaene & Cohen, 2007). The ANS is considered as one of the two core systems for preverbal number presentation, with the other one representing small numbers between 0 and 3. How non-symbolic numerical magnitude processing relates to individual differences in symbolic number learning and later mathematical performance is an open question (DeSmedt, Noel, Gilmore, & Ansari, 2013; Starr, Libertus & Brannon, 2013). Some studies indicate that individual differences in the precision and acuity of representations within the ANS in infancy predicts numerical performance in preschool years as well as future math performance in school (Halberda, Mazzocco, & Feigenson, 2008; Starr, Libertus, & Brannon, 2013). Children with dyscalculia, who exhibit severe deficits in math, also reveal poorer ANS acuity than their TD peers (Mazzocco, Feigenson, & Halberda, 2011). Because current evidence relies on correlational data, whether relations between ANS acuity and math performance indicate causal relations remain unknown. Studying children with PL with different cognitive profiles could reveal if the non-symbolic performance and math performance always go hand in hand, or whether there are cases where the two dissociate. To our knowledge, no existing study examined non-symbolic skills in children with PL. Examining how non-symbolic, symbolic, and mathematical skills develop in children with PL might provide information regarding whether these systems go hand in hand when developmental systems are subject to perturbation.

Summary

Compared to the research on domain-general cognitive performance and language-literacy of children with PL, less is known about their performance in specific skills related to STEM. What might be the implications of the research reviewed above for children with PL's STEM-related skills? STEM-related skills share many commonalities with domain-general cognitive skills and language-literacy skills. Given the close ties between the cognitive and language-literacy skills reviewed above and STEM-related performance, one could expect similar findings – overall great plasticity, stronger role of lesion size, type, and timing than lesion site.

Alternatively, one could expect a different profile for the development of STEM skills. The ontogenetic and phylogenetic roots of language-literacy skills overlap but are distinct from spatial-numerical skills. Further, given their extended developmental trajectory, one could expect more limited plasticity for STEM skills. For example, further research is needed to better understand how children with PL transition through sensitive periods with special importance (such as adolescence or peak periods of synaptogenesis). Although longitudinal studies have been carried out, quality of life in relation to cognitive dysfunctions in adulthood have not been extensively studied. A few longitudinal studies highlight possible cognitive decline in children with PL (e.g., Banich, Levine, Kim, & Huttenlocher, 1990). Some of prior findings are hard to interpret due to possible confounding effects of ongoing seizures and epileptic medications rather than the effect of lesions per se. Given their extended trajectory of development, similar decline could be observed for STEM related skills as well.

As there is scarce research on STEM skills in children with PL, it would be premature to highlight existing similarities and differences across the different domains. Yet, the current evidence suggests that both similarities and differences might exist. Similar to the existing body of research in other domains, lesion characteristics play an important role in children with PL's STEM performance as well. However, children with PL exhibit profiles more parallel to adults with similar injuries in the domain of spatial skills compared to the domains of language-literacy or EF. In particular, site-specific differences might be more apparent for spatial skills. As highlighted in the prior literature, both in spatial and mathematical domains, children experience a slight delay in getting their skills off the ground. Yet, children's deficits are milder than the ones found in adults, they can better compensate for their impairments and catch up with their peers. Although, to our knowledge, only one study examined environmental effects in a STEM-related domain, those findings suggest that environmental factors might play an important role for STEM-related performance (Glenn et al., 2017).

Future Directions

In the last section of our review, we take a future-oriented approach and highlight possible areas of research that would contribute to our understanding of children with PL and plasticity of the developing brain. First, our understanding of development for different cognitive skills in different domains is still limited. As discussed above, little is known about children's cognitive development in STEM related domains. Addressing this question will require considering both differences across domains and different challenges presented in each domain over development. Given its extended trajectory, studying STEM would enable us to assess how the effects of early brain injury are displayed in early versus late childhood. The challenge in answering such questions is finding comparable tasks that could be longitudinally applied at different ages as well as examining performance on age-appropriate novel tasks that assess new challenges children face as they get older.

Our knowledge of child development is also limited at the other end of the time scale, during very early years. As discussed above, the roots of individual differences in STEM skills go back as early as infancy (Halberda, Mazzocco, & Feigenson, 2008). Although the majority of the literature on children with PL leveraged standardized tests, our understanding in the early years, especially infancy, could be enhanced by experimental studies. A few studies on children with PL's spatial development suggests that even when performance is comparable, the process by which children with PL complete spatial tasks might differ from TD children (e.g., Stiles, Reilly, Paul, & Moses, 2005). Experimental studies would shed further light on differences in processing. How children with PL perform in infancy and toddlerhood could also address theoretical questions in the field, such as questions regarding relations among verbal, spatial, and mathematical skills or questions regarding the relations between symbolic and non-symbolic skills in mathematics. The two sets of skills tend to go hand in hand in typical development, which renders it hard to establish causal relations. In the case of children with PL who experienced localized injuries, it might be possible to test which neural systems are necessary and/or sufficient for optimal development in these different areas and how perturbations to one system would influence development in other systems.

Development is not static. Echoing words of late Karmiloff-Smith (1992; 2012), taking static snapshots of children at different ages does not constitute a developmental approach. Especially, in the case of children with PL, the neurocognitive systems face a perturbation and might be expected to be in flux to greater degree than they are in TD. Further, children with PL and TD children might reach the same endpoint by following different trajectories. Findings supporting this view in the domain of reading and spatial development have been discussed above. Thus, it is crucial to examine development of children with PL longitudinally. Similarly, the majority of the research uses standardized or experimental measures of children's performance. How brain injury influences learning mechanisms is not known. Examining different forms of learning might inform our understanding of the underlying mechanisms that contribute to one's performance in each domain.

A small but growing body of literature highlights the importance of examining environmental factors in children with PL's development. The individual variability across TD children at the neural level is limited. Because children with PL have much wider variability in their neurobiological characteristics, they offer insight into how environmental factors interact with children's neurobiological characteristics. An emerging literature with a small number of studies suggest that parental input plays an important role in children with PL's development similar to their role in TD children's development. Prior findings also suggest that parental input might even play a stronger role for tasks that are challenging for children with PL (Rowe et al., 2009; Demir et al., 2015). Future work should examine whether the contribution of environmental factors differ for skills related to STEM. To our knowledge, only one study reported significant effects of parental number talk on children's school entrance math achievement in children with PL (Glenn et al., 2017).

To our knowledge, almost nothing is known about cross-linguistic, cross-cultural differences in children with PL's development in general, and in STEM in particular. The majority of the work in children with PL comes from Western societies speaking Germanic languages. This is surprising in that cross-cultural and cross-linguistic differences have been highlighted in spatial and math development of TD children (Prado et al., 2013), teaching of STEM (Richland, 2015), and in adults with brain injury (e.g., Bates, Wulfeck, & MacWhinney, 1991). Future work should compare the development of STEM related skills in children from different cultures speaking different languages. This research might enable us to disentangle universal versus language-specific strengths and weaknesses in children with PL.

Another area of research is the role of gestures in performance in STEM. Gestures afford representation of dynamic, visuo-spatial information with the hands in three-dimensional space. Gestures have been shown to play a facilitative role for individuals' performance on a wide-range of STEM related tasks such as math equivalence problems (Goldin-Meadow, Cook & Mitchell, 2009), gears tasks (Perry & Elder, 1997), and chemistry tasks (Stieff, Lira & Scopelitis, 2016). Only a handful of studies examined the role of gesture in children with PL and they primarily focused on language development (e.g. Sauer, Levine & Goldin-Meadow, 2010). Whether gesture could play an equally facilitative role for children with PL's STEM performance is not known. Multiple alternatives are possible. If STEM tasks place harder demands on children with PL, gesture might play even a stronger role in children with PL's learning compared to TD children. Alternatively, given their limited performance, children with PL might not be able to benefit from the representational information provided in gestures to the same extent as their TD peers. Further, examining the role of gestures in children with PL can also address theoretical questions in the field of gesture, regarding the interaction between of linguistic versus visuo-spatial factors in gesture processing.

In the current review, we primarily focused on behavioral findings. Indeed, very few studies have examined the structural and functional basis of cognitive development in children with PL (e.g., Fair, Brown, Petersen, & Schlaggar, 2006; Raja Beharelle et al., 2010). Neuroimaging studies are valuable to reveal the neurocognitive systems that might support optimal development in the face of injury. Two children might perform the same on behavioral tests but the underlying neurocognitive systems that support their performance might differ. Going forward, combining behavioral measures with neuroimaging measures would uncover the underlying mechanisms of cognitive development and how they vary in the face of an injury.

Conclusion

To summarize, children with PL present a unique opportunity to examine plasticity in the developing brain. Existing research on children with PL primarily focused on their language, literacy, and overall intellectual functioning. This body of work highlighted the remarkable plasticity of the brain. However, many questions remain unanswered about children with PL's development that would inform our understanding of the developing brain. In particular, examining children's development in domains relevant for STEM would provide both practical and theoretical advances. During the last 50 years, findings from psychology, biology, neuroscience, and medicine have contributed to our understanding of the brain development and its plasticity. Many of these important findings have been shared in Developmental Psychobiology. Our hope is that in the next 50 years, the continued study of children with PL will further inform our understanding of the developing brain and its plasticity.

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