Translating Neurodevelopmental Findings Into Predicted Outcomes and Treatment Recommendations for Language Skills in Children and Young Adults With Brain Injury

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Traumatic brain injury (TBI) accounts for approximately 2.5 million hospital visits annually—nearly half a million for children. At least 5.3 million people in the United States live with chronic disability following brain injury. Deficits in language can result even from mild brain injuries, altering the trajectory of language and social development in injured children. Previous research has observed specific effects of brain injury on language ability across various domains, from single words to sentences, discourse, social skills, and pragmatics. Recent developments in neuroanatomy and neurophysiology provide an increasingly informative framework for developing treatment recommendations in both children and adults with brain injury. This paper first summarizes recent literature on neuroanatomical and physiological changes relating to language development during maturation. Then, the authors reconcile apparent conflicting observations regarding outcomes from brain injury in children and adults. This resolution provides a basis for recommendations for clinical management across the life span for individuals with TBI and for recommendations for future treatment research.

What is the significance of this article for the general public?

Recent developments provide an increasingly informative framework for defining cognitive-linguistic treatment recommendations in both children and adults with traumatic brain injury. In all cases, measurable improvement depends largely on type, location, and extent of damage, as well as individual factors, leading to clinical approaches that involve trial of multiple evidence-based strategies.

Keywords: language, development, brain injury, treatment

Traumatic brain injury (TBI), or acquired injury to the brain due to sudden trauma, has garnered recent attention as a pressing public health concern that accounts for approximately 2.5 million hospital visits annually (Langlois, Rutland-Brown, & Wald, 2006). Even minor TBI in childhood can be consequential, particularly as children are still rapidly acquiring language and cognitive skills. Even a deficit that lasts only a few weeks can have a major impact on a semester-based educational curriculum. This paper will summarize current literature on neuroanatomical and physiological changes relating to language deficits following closed head TBI, along with language development during maturation, in order to provide concrete recommendations. Discussion of changes and recommendations will focus on mild to moderate injury severities, as these are the most common (Centers for Disease Control and Prevention, 2014).

Effects on language can have a profound impact on education and social growth and may fundamentally alter the trajectory of development (Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; Ponsford et al., 2001). While some individuals appear to recover fully on standard-

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ized measures in the weeks following a TBI, others experience diverse, prolonged deficits and extreme distress (Anderson et al., 2012; Ponsford et al., 2001). Persistent impairments are most common among children who have had prior head injuries, preexisting learning difficulties, neurological or psychiatric problems, or family stressors. However, children with early TBI demonstrate more consistent language impairment than similarly injured older children (Ewing-Cobbs & Barnes, 2002; Shaffer, Bijur, Chadwick, & Rutter, 1980; Wrightson, McGinn, & Gronwall, 1995). TBIs during young adulthood appear to have the best outcomes, with both infants and older adults (over 55 years of age) having the poorest recovery (Ewing-Cobbs & Barnes, 2002; Shaffer et al., 1980; Wrightson et al., 1995).

Effects of TBI on language ability occur across various domains, from single words to sentences, discourse, social skills, and pragmatics in individuals with mild, moderate, or severe injury (Carroll et al., 2004). In general, individuals with TBI have more difficulty producing language than understanding language used by others. They demonstrate decreased expressive language, poor auditory selective attention, increased reaction time, and difficulty in working memory tasks involving language production (Bonnier, Marique, Van Hout, & Potelle, 2007; Ewing-Cobbs & Barnes, 2002). The most commonly reported problem is anomia: difficulty naming objects or people that are perceived correctly (King, Hough, Walker, Rastatter, & Holbert, 2006; Ylvisaker, 1986). Individuals with TBI may have difficulty understanding language, including written stories, which has been linked to word identification and processing deficits (Barnes, Dennis, & Wilkinson, 1999).

Deficits can also be observed at the interface between disrupted language and broader cognitive challenges, such as working memory, executive function, or core cognitive capacity (Ganesalingam et al., 2011; Gerrard-Morris et al., 2010; Moran & Gillon, 2004; Sullivan & Riccio, 2010). Speed of processing is affected across domains, perhaps implicating deficits in several aspects of information processing (Boll, 1983; Haut, Petros, Frank, & Haut, 1991; Tromp & Mulder, 1991). The cognitive– linguistic domain—those linguistic skills that are interwoven with domain-general cognitive skills—is of particular importance in TBI, as deficits in this domain have been observed in even the mildest injuries (Gerrard-Morris et al., 2010; Papoutsis, Stargatt, & Catroppa, 2014).

Although some of these deficits can occur following an injury at any age, some seem to be particularly severe in children, and deficits in children also uniquely emerge long after the injury itself (Ewing-Cobbs, Barnes, & Fletcher, 2003; Ewing-Cobbs et al., 2006). One reason for this may be that children's brains are still maturing, and thus earlier insult can impact the process of development. The young brain is fundamentally different from the mature brain, both structurally and functionally (Giedd et al., 2015; Karmiloff-Smith, 2009). The following sections discuss what is known about brain maturation; a discussion of the process of brain recovery also follows.

Structure and Function Changes in the Brain and Implications for TBI

Improvements in language co-occur with anatomical and physiological *maturation*, or the emergence of adult characteristics over time. Development occurs in different regions at different rates (Sowell et al., 2003); language development begins in utero (Moon, Lagercrantz, & Kuhl, 2013) and continues into early adulthood. The infant brain is highly interconnected and coarsely coded, but it gradually changes to reflect localization and specialization driven by three maturational processes: synaptic proliferation, synaptic pruning, and myelination change (Giedd et al., 2015; Goddings et al., 2014). Proliferation-the creation of new neural connections—occurs at the rate of approximately 60 million new connections per day in early life and is followed by a period of pruning, where infrequently used connections are eliminated and frequently used connections are strengthened, building toward adult levels of neural connectivity (Blakemore & Choudhury, 2006). White-matter volume increases with age (Sowell et al., 2003), reflecting increased connectivamong spatially disparate regions ity (Karmiloff-Smith, 2009). Myelination influences plasticity by releasing factors that inhibit axon sprouting and creation of new synapses (Giedd et al., 2015). Regionally specific changes in white-matter organization correlate with improvements in language (O'Muircheartaigh et al., 2014), reading (Deutsch et al., 2005), and domain-general skills such as memory (Nagy, Westerberg, & Klingberg, 2004).

Cortical regions associated with language mature relatively late, corresponding to the observation that language skill development is protracted over the life span (Sowell et al., 2003). Language milestones occur on a backdrop of increasing lateralization and specialization. Language lateralization in the left hemisphere begins at approximately three months of age and continues through age 5 in healthy children (Ilves et al., 2014; Ressel, Wilke, Lidzba, Lutzenberger, & Krägeloh-Mann, 2008). Beginning in primary school, the knowledge of words and their meanings is reorganized from a system built on a foundation of memory and recall of single units to a system based on relationships among units (Cronin, 2002) to facilitate efficiency.

In very young children, damage to the brain may result in more diffuse cognitive–linguistic deficits, reflecting damaged coarse underlying representations. Deficits emerging later in life may be explained by difficulty learning skills that rely on a foundation of other skills or by the inability to keep up with increasing environmental demands (Anderson, Spencer-Smith, & Wood, 2011). In contrast, mild injury in later teenage and adult years may have little apparent long-term effect on discrete skills, although deficits in efficiency may still be measurable (King et al., 2006).

Plasticity Changes in the Brain and Implications for TBI

As children mature into adulthood, brain structure and function change. Plasticity-the ability to adopt new functional or structural states (Ganguly & Poo, 2013)-changes during maturation and is influenced by heredity and environment. Plasticity in adults is characterized as experience dependent in contrast to experience expectant, which characterizes plasticity in infants and young children (Huttenlocher, 2009). Experience-expectant plasticity requires specific experiences to drive the development of related cognitive abilities. If a brain injury denies a young child the ability to have certain formative experiences, then processes can be derailed early in life (Kolb & Gibb, 2014). In contrast, experience-dependent changes require a *mismatch* between functionality and an external force that drives functional and structural change (Elman et al., 1998; Lövdén, Bäckman, Lindenberger, Schaefer, & Schmiedek, 2010). This forms the basis for learning new skills as well as recovery from TBI (Ganguly & Poo, 2013), as individuals are challenged by their environment to regain lost skills.

Anatomically, young brains have unspecified synapses and dendritic connections that allow for increased flexibility to transfer and reorganize functions (Karmiloff-Smith, 2012), even overcoming localization biases (Bates, Dale, & Thal, 1996; Eisele & Aram, 1996). However, the same mechanisms underlying recovery also dictate its limitations (Anderson et al., 2009). For example, inappropriate connections may be established (Stein & Hoffman, 2003), resulting in dysfunctional recovery (Aram & Eisele, 1994). Despite the early suggestion that less discrete commitment in the young, plastic brain allowed it to adapt more readily to damage than the adult brain (Eisele & Aram, 1996; Reilly, Bates, & Marchman, 1998), this notion has largely been disproved (Daneshvar et al., 2011; Lloyd, Wilson, Tenovuo, & Saarijärvi, 2015; Satz et al., 1997). The first year of life is associated with the greatest neural plasticity, and children with perinatal lesions consistently have the poorest functional outcomes (Anderson et al., 2009; Ewing-Cobbs et al., 1997). Cognitive-linguistic impairments persist in the pediatric population following injury (Ewing-Cobbs et al., 1997; Fay et al., 2010); that is, while children may be better able to transfer and reorganize brain function, leading to resolution of skills they may have lost, they do not appear to show normal language development thereafter.

These outcomes may be a consequence of critical- or sensitive-period plasticity (Ganguly & Poo, 2013; White, Hutka, Williams, & Moreno, 2014), in which skills are differently vulnerable over maturation. During a sensitive period, underlying neural mechanisms are coarsely specified and sensitive to input, and learning is primarily driven by bottom-up processes triggered by exposure (White et al., 2014), leading to these periods being associated with both the best and the worst outcomes for language after injury (Anderson et al., 2011). One such period in the development of language (Werker & Tees, 2005) is the vocabulary burst observed at approximately two years of age

(Anderson et al., 2011). If the child receives rich language input during this period, neural circuits underlying language will establish robust representations of specific features of the language (Scott, Pascalis, & Nelson, 2007), leading to more refined, adult-like language usage (White et al., 2014). However, if a child has a TBI during this period, cognitive impairments may persist through adolescence to adulthood (Fay et al., 2010), affecting executive function, verbal intelligence, and expressive language function (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Catale, Marique, Closset, & Meulemans, 2009; Ewing-Cobbs et al., 1997).

Mechanisms for Recovery and Implications for Clinical Intervention in Adults

The processes driving recovery in brain structure and function are different in adults and children. In adults, these processes are relatively well understood at the cellular level (Burda & Sofroniew, 2014; Nudo, 2013). Recovery involves restoring and substituting structures and functions (Anderson et al., 2011) and occurs through branching of injured and uninjured neurons and resolution of disrupted functions away from the site of injury. Traditional behavioral therapy approaches to rehabilitation following injury support processes associated with substitution of function. Methods of supporting restitution, or rebuilding of cells and connections through regeneration and sprouting, are still emerging. Restitution occurs automatically through slow and limited biological processes of recovery (Delgado-García & Gruart, 2004), but researchers are exploring techniques that directly manipulate the underlying cortical nerve cells-for example, by using repeated electrical stimulation to alter the threshold for exciting a region long term (Pape, Rosenow, & Lewis, 2006). When paired with intensive training, these techniques may lead to improved performance in language and cognitive rehabilitation over training alone (Baker, Rorden, & Fridriksson, 2010; Grefkes & Fink, 2012). Therapeutic interventions targeting restitution appear promising and may provide added benefit during recovery.

In substitution, uninjured regions may functionally take over an injured area through unmasking of preexisting inhibited functions. While these changes happen spontaneously (Robertson & Murre, 1999), intensive cognitive-linguistic therapy correlates with increased rebuilding of cellular connections within the acute and chronic stages after injury as well as with functional recovery (Schlaug, Marchina, & Norton, 2009). Rehabilitation supporting substitution includes behavioral therapy focused on a specific task with high intensity to exploit activity-dependent neural plasticity for long-term improvements (Cramer et al., 2011; Turner-Stokes, Disler, Nair, & Wade, 2005). Current evidence shows no ceiling effect for therapy intensity, which is associated with earlier, stronger behavioral gains. Further, when substitution is inefficient or maladaptive, it can be corrected. For example, reinforcing speech by constraining compensatory actions such as gesturing or drawing can correct for maladaptive substitution (Meinzer, Djundja, Barthel, Elbert, & Rockstroh, 2005).

Recommendations for therapeutic intervention with adults following brain injury include teaching compensatory strategies for support in participation and activities of daily living (Mayer, Keating, & Rapp, 1986; Shum, Fleming, Gill, Gullo, & Strong, 2011), high-intensity repetitive drills of discrete and specific skills, and dual-task training to increase cognitive complexity (Evans, Greenfield, Wilson, & Bateman, 2009). Combined individual and group therapy incorporating communication partners may provide a good balance between narrow skills-focused and highly functional therapeutic activities.

Mechanisms for Recovery and Implications for Clinical Intervention in Children

In contrast to the mechanisms thought to underlie adult recovery, recovery of cognitive function observed in young brains is likely more influenced by neural regrowth and anatomical reorganization (Giza & Prins, 2006; Kolb, Gibb, & Robinson, 2003). Recent interventions targeting restitution of function in adults are all but unexplored in children, and while treatments used in adults may support substitution-based functional recovery, few language treatment studies in children with brain injury exist. Maturation occurs on a relatively rapid trajectory, making interpretation of treatment effects challenging and requiring that children with TBI be more frequently evaluated during the course of recovery and treatment in order to monitor areas of weakness and reset baselines for measuring treatment effect (Diamond, 2009; Karmiloff-Smith, 2009) as environmental demands increase. Further complicating the treatment recommendations for children are the interconnected nature of language and domain-general cognitive skills during development. Difficulty in memory or attention may appear as deficits in language processing and vice versa. This leads to difficulties isolating the core or most efficient therapeutic target in young children. As the child matures, deficits will become more distinguishable and can be more directly targeted. Yet overlapping difficulties following TBI persist, including aspects of language, cognition, attention, and behavior.

Targeting discrete, highly functional complex language, pragmatic, and social skills may offer the greatest potential long-term benefit for communication and social participation and may be accomplished through expressly relating new information to existing information (Oberg & Turkstra, 1998). Techniques that focus on identifying specific problem areas in daily life and on improving a child's ability to consider his or her own thoughts and engage in problem solving (e.g., cognitive behavioral therapy) may improve executive function skills and behavior (Centers for Disease Control and Prevention, 2014: Kurowski et al., 2013: Slomine & Locascio, 2009), making a child more receptive to therapy targeting academic and linguistic skills. Moreover, technology- and child-oriented styles may increase interest in therapy and improve outcomes (Kaldoja et al., 2015).

In pediatric patients, an additional consideration is the need to support education. Deficits in language and cognition can also impact learning, resulting in the child falling farther behind and having continuing difficulties when returning to school. As such, children with TBI may benefit from additional time and multimodal presentation of language content while learning (e.g., verbally presented classroom instruction paired with prewritten outlines) to accommodate difficulties in rapid processing and decrease demands on both language and cognition in educational contexts (Bowen, 2005; Hux et al., 2010). Optimizing the child's environment may include minimizing distracting sounds and visuals in the classroom (Childers & Hux, 2013); modeling rather than explaining desired skills and strategies; and providing concise, direct instruction when necessary (Hathcote, 2009).

Based on these considerations, recommended therapies in young children may include those that are highly multimodal, tapping many skills at once, rather than only those designed to target specific skills in isolation. If a finite area of deficit is identified, short-term, intensive targeting of that skill may be warranted. Computerassisted and virtual reality modes of therapy may improve motivation and enhance treatment effects (Laatsch et al., 2007). Academic performance following injury should be monitored in the years following return to school. Given that deficits may appear in later years, children may require longer term follow-up than adults. While restitution-based therapies are in the early stages of research for pediatric populations (Friel, Kuo, Carmel, Rowny, & Gordon, 2014; Rocca et al., 2013), it is unclear whether these are advisable (Kadosh, 2014).

There is only limited information with which to evaluate the effectiveness of interventions for children with TBI (Bowen, 2005), and because of differences in plasticity, effective treatment approaches for adults cannot be directly translated to work in children. More longitudinal studies are needed to fully assess how plasticity differences with age interact with recovery and response to treatment. Future research on the rehabilitation of cognitive-linguistic function in children in conjunction with behavioral therapy and pharmacotherapies likely will yield promising results and will continue the trend of increasingly individualized treatment design. Further, individual treatment studies in neuropsychology and cognitive-linguistic speech language rehabilitation are sorely needed to validate and optimize novel and existing treatment strategies and combinations.

Summary and Concluding Remarks

Recent developments in neuroanatomy and neurophysiology provide an increasingly informative framework for deducing cognitive– linguistic treatment recommendations in both children and adults with TBI. Across treatment strategies, measurable improvement depends largely on type, location, and extent of damage, as well as on individual factors, leading to clinical approaches that involve trial of multiple evidence-based strategies (Anderson et al., 2011; Sullivan & Riccio, 2010). However, improvements in our understanding of changes to anatomy and physiology over time will further improve our ability to design cognitive–linguistic treatments for adults and for children who have experienced brain injury at different stages of development.

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