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Organized By: The Brain Recovery Project

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Discussion Summary:

The objective of the second international scientific workshop on brain plasticity, hemispheric specialization, and neuro-rehabilitation after cerebral hemispherectomy was to advance the field of rehabilitation neuroscience by bringing together a cross-disciplinary group of U.S. and international clinicians, educators, researchers, and families affected by hemispherectomy surgery, in a format that would encourage the exchange of information through formal presentations as well as less structure collegial discussions and social gatherings.

The conference offered a keynote presentation on neuroplasticity after childhood brain injury, and a series of presentations from an eclectic mix of researchers which covered a broad range of topics from surgical techniques to acquisition of literacy after cerebral hemispherectomy. Most importantly, this unique workshop – which overlapped with the 2014 Hemispherectomy Conference and Family Reunion - allowed families impacted by hemispherectomy surgery, as well as adults who had childhood hemispherectomy, to interact with researchers both during formal presentations and social gatherings, which provided researchers and families alike with opportunities to discuss the "real world" impact of the procedure throughout the lifespan.

The specific aims of this conference were: to assess our current understanding of how adaptive cortical plasticity can be manipulated to enhance brain recovery in the areas of rehabilitation, neuropsychology,and education post-hemispherectomy; to initiate a collaborative process between survivors, parents, and professionals from multiple fields to determine research goals; to highlight neglected areas of research and establish a research consortium to address clinical deficits, share common data elements, and assess research goals and objectives based on findings; and, to bring together established and young investigators who study neuroplasticity and encourage them to research cortical plasticity post-hemispherectomy

What follows is our summary of the key points presented at the symposium, and includes some of the abstracts (edited) prepared by the presenters.

II. LESSONS FROM CHILDHOOD BRAIN INJURY

Although there is still much to learn about developmental outcomes of hemispherectomy, research on other childhood neurological conditions can help chart the way. Past longitudinal research on the outcomes of early brain injury across the childhood years indicates that several factors are relevant in determining outcome at any one point in time. These factors include the child's age at the time of injury and at assessment, time since injury, and a variety of medical and environmental risk and protective factors.

Because childhood brain disorders affect the course of brain and behavioral development, it is useful to take a long-term, or "life span," perspective. A future-oriented approach can help in determining the most appropriate short-term interventions and in planning for the future. The effects of disorders may persist, but consequences can vary with advancing age. Development is dynamic; children's identities and capacities evolve with new experiences, roles, and challenges.

One advantage of a life span perspective is the possibility of providing the child and family anticipatory guidance during childhood. This perspective can also give adult health care providers insights into the origins of problems that may arise when the individual transitions to adulthood.

Several principles apply in following children with brain disorders across childhood. First, the effects of brain injuries are developmental, with different outcomes and needs at different points along the way. Second, these effects tend to persist in children with more severe brain insults but may also be malleable. Third, assessing a range of cognitive skills (not just IQ) and functional capacities, such as academic achievement, behavior, daily living skills, is critical in understanding the effects of brain disorders and in clinical management. Fourth, these effects are subject to multiple influences, including the type and timing of brain disorder, medical complications, experiences and family and school environments, genetic propensities, and the child's ability to compensate for brain injury by building alternative neural networks or learning how to function in ways that limit dependence on the affected brain regions. Finally, research is essential if we are to find ways to help children become more productive and well-adjusted and to advance knowledge of underlying reasons for adverse effects of development.

Brain disorders can be classified based on age at injury as: (1) genetic and neurodevelopmental disorders, such as Fragile X, learning disabilities, attention deficit hyperactivity disorder, and autism spectrum disorder; (2) perinatally acquired, such as brain abnormalities due to prematurity; and (3) postnatally acquired, including conditions such as postnatal strokes, infections, or traumatic brain injury. Conditions leading to a hemispherectomy may fall into any of these categories. Because development can vary according to age at injury, this factor may be relevant in predicting future outcomes. For example, the effects of neurodevelopmental disorders may not be immediately evident after birth, while acquired brain injuries may have more immediate consequences. In children with post-natal brain injuries, a younger age at injury is associated with greater deficits. While deficits generally persist over time, follow-up can also reveal either decreasing or increasing deficits over time. The child's age at the time of assessment is another factor to consider, as brain injuries may affect later-developing skills more so than earlier-developing ones.

The pattern of developmental changes exhibited by a child following an early brain insult is also related to the type and severity of brain disorder and to environmental factors. Long-term outcomes are worse for children with more diffuse and severe brain insults, with neurological complications such as seizures, or with physical disabilities that limit activities important for ongoing skill development. Other risk factors include developmental problems prior to an acquired injury, genetic variants that are less optimal for neural recovery, and environmental factors such as the family's resources, family dysfunction and burden, and ineffective parenting styles.

Little is known about the reasons for environmental influences on recovery after brain injury, but research suggests that more positive family environments contribute to better outcomes.

Some neural reorganization is possible following brain insults. Brain plasticity is activity dependent in the sense that it occurs in response to experience and exposure to new learning opportunities. Plasticity early in life is facilitated by over-production of neurons, subsequent “pruning,” and potential for “re-wiring” as illustrated by occipital involvement in learning of Braille with early blindness, shift of language to right hemisphere in cases of early damage to left hemisphere. Compared to the developed older brain, the younger brain is therefore more sensitive to environmental enrichment. However, the young brain is also more vulnerable to deprivation/stress, and early plasticity has the potential to be maladaptive as well as adaptive. The potential for greater neural reorganization following early brain insults is additionally constrained by the specialization of some brain regions for specific functions even early in life (e.g., higher-level language processing in left hemisphere and spatial processing in the right hemisphere). Further constraints on early plasticity are suggested by evidence that widely distributed brain regions contribute to later specialization of function, which implies that the loss of brain tissue, even early in life, may be disadvantageous for longer-term cognitive development.

Research on developmental outcomes of hemispherectomy may be guided by past studies of other brain disorders, such as spina bifida meningomyelocele (SBM) and extreme prematurity. SBM is a defect in closure of neural tube with hydrocephalus, dysgenesis of the corpus callosum, and damage to posterior brain regions. Extreme prematurity is defined by <28 weeks gestational age or <1000 g birth weight and is frequently accompanied by brain injuries to white matter such as periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and reductions in brain volumes. Studies of these two conditions demonstrate the value of in-depth assessments of cognitive and academic strengths and weaknesses, longitudinal follow-ups through early adulthood, and examination of medical and environmental risk factors. For example, research on children with SBM has revealed more problems in higher-level language skills, such as making inferences, than in lower-level abilities such as word reading—findings that are useful in planning interventions for these children. Studies of both SMB and extreme prematurity have also revealed specific patterns of cognitive changes over time, identified medical and environmental risk factors, and provided data on adult outcomes. This information is useful in counseling children and their families, identifying the children at highest risk for problems, and targeting interventions to optimize longer-term adaptation.

Applying these research strategies to children with hemispherectomy will enhance our understanding of variations in outcomes and the factors related to these variations, as well as how best to assess the children and identify their needs. However, we have a strong start as we already know a good deal of clinically useful information about the conditions that lead to hemispherectomy, medical risk factors, and outcomes before and after surgery. This research documents the benefits in stopping or reducing seizures, with some positive effects for most children and suggests that there is substantial variability in outcomes but with mildly impaired cognitive abilities overall. Past studies also indicate that outcomes vary across different conditions, with better outcomes associated with vascular lesions (perinatal stroke, Sturge-Weber) and Rasmussen's encephalopathy than with cortical dysplasia. For children with Rasmussen's encephalopathy, research suggests that there is some risk for post-surgery reduction in expressive language and that language abilities and IQ are generally lower with left compared to right hemispherectomy. Some children show impressive language recovery following surgery. Although these positive outcomes were once thought to require surgery at a younger age, when shift in language dominance was more likely, a number of studies have found good outcomes even after later surgeries. Little research has been conducted to examine the effectiveness of interventions after surgery, though de Bode et al. have demonstrated positive effects of motor training.

We thus have much to learn about the consequences of hemispherectomy and the conditions leading to these surgeries, as well as about predictors and evidence-based interventions. Future directions for research in this area will include efforts to fill these gaps in knowledge by investigating the nature, variability, and predictors of cognitive-behavioral outcomes post hemispherectomy. Areas of special interest will be on specific types of language and spatial skills most affected and on other outcomes that have not been comprehensively assessed, such as executive functioning, academic achievement, behavior adjustment and social skills, and reward sensitivity. Research examining associations of cognitive outcomes with the status of the remaining hemisphere, using measures of brain structure (MRI), neural activation (fMRI and PET), and neural connectivity, may be useful in explaining variations in outcomes and in identifying compensatory neural systems. Other clinically relevant questions for future research include the optimal timing of surgery, reasons for generalized cognitive deficits, and the role of genetic factors in predicting outcomes. Additional research directions include investigation of developmental trajectories and transitions to adulthood, and exploration of ways to optimize activity-dependent plasticity in motor and cognitive skills, functional independence, and quality of life. Such research will provide the type of information needed to anticipate future needs, guide developmental and educational interventions, and increase our understanding of factors related to neural plasticity.

III. FACTORS THAT AFFECT FUNCTIONAL OUTCOMES

It is important to note that not all cases of cerebral hemispherectomy are the same. Differences in techniques, underlying etiology, and timing of initial injury and seizure onset are only some of the several factors which affect functional outcomes. Researchers must understand this inherent variability in order to properly plan experimental protocols that will yield interpretable results.

A. SURGICAL TECHNIQUES

Surgical techniques vary by how much of the cortex is removed (partial or complete) and whether deeper structures such as the basal ganglia and thalamus on the affected side are resected. Many surgical facilities have abandoned anatomic hemispherectomy because surgical complications such as excessive blood loss, or late complications such as onset of superficial hemosiderosis or hydrocephalus even many years after surgery. Even with these concerns, some facilities continue to use anatomical hemispherectomy especially in cases of hemimegalencephaly.

Several techniques for hemispherectomy have evolved where the cerebral hemisphere is deafferentiated while vascular supply is preserved. These techniques replace the classic hemispheric resection (true anatomical hemispherectomy) which has the disadvantage of leaving a large resection cavity giving rise to long term complications. The broad range of procedures, from true anatomic hemispherectomy to the vertical parasagittal hemispherotomy, which removes very little cortical tissue, is just one factor that affects outcomes.

B. ETIOLOGIES

The most common etiologies leading to hemispherectomy include a prior history of brain injury (perinatal stroke, trauma, infection), cortical malformations (hemimegalencephaly, other cortical dysplasias, and neuronal migration defects), and inflammatory conditions (Rasmussen encephalitis). Some of these etiologies may impact not only the hemisphere producing seizures but the contralateral "healthy" side. For example, hemimegalencephaly is one condition that sometimes has bilateral cortical involvement. It can also be part of an overall syndrome, including megalencephaly capillary malformation syndrome, that can include other brain malformations (such as Chiari malformation) and physical abnormalities such as Proteus syndrome and congenital infiltrating lipomatosis. The most severe form of cortical dysplasia, hemimegalencephaly often includes polymicrogyria and overgrowth of neuroglial tissue into the subarachnoid space, as well as immature neurons.

Timing of lesion acquisition is of paramount importance. The maturation of brain pathways is a non-linear process that differs considerably according to brain region. Prenatal life is a period of particularly rapid brain growth; cortical malformations can arise prenatally throughout gestation and are a primary pathological substrate for focal and hemispheric dysfunction and intractable epilepsy. Cortical malformations carry unique implications for brain organization and functionality as they influence primary neural specification rather than following the postnatal model of deficit and post-injury reorganization.

C. AGE OF SEIZURE ONSET AND AT TIME OF SURGERY

Hemispherectomy and other radical surgical procedures for treating pharmaco-resistant focal epilepsy trigger significant concerns about postoperative functionality and quality of life. While brain lesions acquired in childhood are generally assumed to be less deleterious due to superior functional recovery compared to lesions acquired in adult life, this conclusion is undoubtedly an oversimplification. It is more realistic to conceptualize brain lesions acquired in early life as having a different set of consequences compared to similar lesions in the fully mature brain. The factors responsible for these age-related differences are complex, show considerable overlap and often produce findings that appear contradictory. We know that seizures in infancy can profoundly impact later development.

Neuroplasticity further depends on the age at surgery. Depending on the surgical center, etiology and type of operation may impact if children become seizure free after surgery.

D. ANTI-EPILEPTIC DRUGS

It is important to note that nearly all of these children have been exposed to anti-seizure medication at different time points of postnatal brain development. These clinical variables all need to be considered when planning studies involving patients after cerebral hemispherectomy in order to understand the possible contribution of what was removed, etiology, and timing of brain injury related to development neuroplasticity.

E. NEURAL NETWORK ORGANIZATION

Neural network organization is a critical factor to consider. Most cognitive networks are widespread and have both ipsilateral and contralateral connections in the typically-developing brain. These networks, also known as connectomes, constitute the operational substrates of cognitive and sensorimotor processing and a disturbance can lead to functional deficit which may be permanent. It is likely that correlating lesion size to functional outcome is more likely measuring selective network disruption rather than absolute volume of removed tissue. Certain nodes are more critical to network functionality. Furthermore, neural network dysfunction may arise either from anatomic lesioning or from epilepsy-induced functional disturbance.

F. FUNCTIONAL RESERVE

Functional reserve, particularly with regard to adequacy of the contralateral cerebral hemisphere, exerts a strong influence on functional outcome. Functional reserve is strongly correlated with pathological substrate and some pathologies are more likely to be bi-hemispheric, a situation which diminishes contralateral functionality. Thus, the concept of recovery from unilateral damage due to the “intactness” of the contralateral hemisphere implies both an absence of pathological involvement and fully functioning contralateral network nodes.

Future research needs to focus on all these factors, but particularly on brain maturation (timing) and neural network organization. Further refinements in our understanding of these issues should produce a more comprehensive picture of brain maturation and generate strategies for maximizing non-seizure outcomes after radical epilepsy surgery.

IV. MOTOR RECOVERY

A. THE IMPORTANCE OF SENSORY INPUT

Brain development begins with conception and continues well into the third decade of life. During this development there are several periods that the response to cerebral injury is better than at other times, and this varies with the type of injury. Focal injuries differ from removal of an entire hemisphere, likely because with focal injuries there are extensive changes in the damaged hemisphere and limited change in the intact hemisphere whereas after hemispherectomy there are extensive changes in the remaining, intact, hemisphere.

In hemispherectomized rats, the extent of plastic changes in the intact hemisphere are greater the earlier the surgery is performed. The most obvious plastic responses in the intact hemisphere are an increase in cortical thickness that is related to increasing complexity of the cerebral neurons, and possibly the number of cortical neurons, as well extensive rewiring of corticofugal pathways. These pathways act to enhance motor skills of the forelimbs and forepaws on the affected side. The earlier the hemisphere removal the larger these effects are. Any damage to the unoperated hemisphere compromises these plastic changes.

Hemispherectomy at any time during development can be modified by post-surgical treatments, especially including tactile stimulation beginning shortly after the surgery. For example, light tactile stimulation three times per day (fifteen min each) is sufficient to enhance both motor and cognitive outcomes in adulthood. Placing animals in complex, interesting, environments is also beneficial although this experience is no more effective than the tactile stimulation, likely because the tactile stimulation can begin much sooner. Nonetheless, the data show that outcomes can be enhanced by behavioral therapy regardless of the age at which it is begun.

B. INTENSIVE REHABILITATION IN THE ACUTE RECOVERY PHASE

Acute multidisciplinary inpatient rehabilitation is often recommended after hemidisconnection surgery. Although inpatient rehabilitation has the potential to improve recovery trajectory and thus outcomes, there are no studies to date examining the efficacy of acute rehabilitation in children after hemidisconnection.

One study examined 22 children who underwent acute inpatient multidisciplinary rehabilitation after hemispherectomy. The program included a minimum of 3 hours per day of Occupational Therapy, Physical Therapy, and Speech/Language Therapy, as well as consultation through Neuropsychology, Behavioral Psychology, Nutrition, Therapeutic Recreation, Social Work, and Audiology. The average age at admission was 8.1 years. Children were admitted to the program an average of 12.6 days post-surgery, and participated in the program for an average of 27.6 days. Children with acquired etiology (Rasmussen Encephalitis) tended to be older and stay in the program longer than children with congenital etiologies. Children were evaluated at admission, discharge, and 3 months post-discharge using the Functional Independence Measure for Children (WeeFIM®), an 18 item measure of self-care, mobility, and cognitive function. The average level of functional independence at admission was approximately 30% "normal" for age, with both etiology groups at a similar level. Overall, the children made significant gains ($p<.01$) from admission to discharge across all three domains. Interestingly, children also made significant gains ($p<.001$) from discharge to 3-month follow up. Average gains during the program did not differ between etiology groups; however, the acquired group made significantly greater gains during the 3-months after discharge, reaching a level of close to 85% "normal" functional independence for age.

While these findings are promising, the amount of functional gain expected during this time period for children who do not participate in rehabilitation was not examined, so the impact of the intervention is not clear. Rehabilitation interventions, including the timing of treatment, duration of treatment, and sustainability of gains need to be studied more comprehensively in order to determine the best treatment approaches to maximize recovery and long term outcomes after surgery.

C. EMERGING THERAPIES FOR BRAIN REPAIR – LESSONS FROM ISCHEMIC STROKE RECOVERY

Brain repair can be defined as the process of restoring brain structure or function after injury. Repair can be innate or driven by exogenous therapy. Many forms of repair-based therapies are under study. These include growth factors, other large molecules such as monoclonal antibodies, numerous small molecules, cell-based therapies, robotic devices, devices focused on brain stimulation, and telehealth methods. Each has its relative areas of strength and of concern.

For example, recently it has been shown that the selective seratonin reuptake inhibitor fluoxetine improved motor deficit in adult patients with ischaemic stroke and hemiplegia which appeared to be independent of the presence of depression. Should they thus be used in the acute phase after hemispherectomy? Growth factors have very powerful neurotrophic actions, many are large molecules that do not cross the blood brain barrier. Stem cells show enormous potential in preclinical models, but their translation may be affected by safety, ethics, or regulatory concerns. Robotic devices can deliver therapy with enormous precision, can measure patient performances, and can be programmed in myriad ways; however, task ecology may not be desirable, it remains unclear how which devices are best for which patients, and many robotic devices are too expensive for most individual patients.

Methods that emphasize intensive physical and/or cognitive practice are of double value. First, these are useful in their own right as an intervention to improve behavioral outcomes. Second, such activities are key adjuvants, shaping effects of restorative therapies, which improve patient outcomes on the basis of experience-dependent brain plasticity.

A major consideration in the development of restorative therapies is the need to match the right patients with the right therapies. Many factors influence outcome and response to restorative therapies. For example, age can be a critical covariate, whether comparing infants with 4 year-olds, or teens with 80 year-olds. Details of neural injury can also be key, for example, massive injury vs. minor and focal injury, or injury that severs most of a major tract vs. less than half. Medical comorbidities can also play a critical role, such as presence vs. absence of diabetes mellitus, or of autism. Concomitant therapies may also be important covariates for understanding effects of restorative therapies, for example, high doses of sedating drugs could impact effects of therapies targeting brain repair. Understanding how such inter-subject differences affect response to a restorative therapy is a critical consideration that needs to be understood in parallel with development of new therapies. Such details influence the likelihood of response to a restorative therapy and so may be useful for patient stratification.

C. THE ROLE OF MIRROR NEURONS IN REHABILITATION

Mirror neurons are a special class of cells in the cerebral cortex. They were originally discovered in the ventral premotor cortex of the macaque brain. These cells fire while the subject is performing actions that are typically intentional and goal-oriented, such as grasping an object, biting a piece of food, making a facial expression, orienting the eyes toward an attentionally salient stimulus. Mirror neurons also fire while the subject is not performing these actions, but is simply watching, without moving, someone else performing the same actions or actions that achieve the same goal. These cells are thought to compose a system in the brain, called the mirror neuron system (MNS), that matches the perceptual aspects of the actions of other people onto the motor plans of the observer.

The MNS has been associated with a number of important cognitive functions, including observational and imitative learning. Brain mapping studies in humans suggest that the MNS is fairly equally represented in the two cerebral hemispheres. This suggests that the functional properties of the MNS may be potentially used in hemispherectomy to accelerate motor recovery. Indeed, studies show that action observation in addition to physical therapy improves motor recovery in brain damaged patients, compared to physical therapy associated with some other control interventions.

A key issue in planning interventions for motor recovery, however, is to determine individual differences in neural plasticity. These individual differences may suggest the amount of intervention required by each individual patient, providing a marker for personalized interventions for motor recovery. Ongoing studies are investigating these individual differences. Two promising potential classes of markers of plasticity can be obtained with non invasive neuromodulation and with brain imaging.

Transcranial Magnetic Stimulation (TMS) stimulates the brain non invasively, by producing over the scalp a rapidly varying magnetic field that induces an electric current in the brain. Markers of TMS-induced neural plasticity may potentially be useful in differentiating individuals with high and low level neural plasticity. Furthermore, effective interventions are likely to influence a number of neural systems that may be integrated in large networks through anatomical and functional connectivity. Hence, magnetic resonance imaging (MRI) techniques that can measure anatomical (diffusion weighted imaging, DWI) and functional (resting state functional MRI) connectivity may also help assessing individual differences in plasticity. These two classes of markers of plasticity, TMS- and MRI-based, when combined, may provide a powerfully rational approach to the complex problem of stratifying patients for interventions.

Lastly, the MNS has also been implicated in language and its learning. Thus, the logic applied above to motor recovery can in principle be applied also to the case of recovery of language functions in hemispherectomy.

V. SENSORY CHALLENGES

A. Neural Substrates of Blindsight

Hemispherectomy subjects offer a unique opportunity to study the role that subcortical structures play in blindsight because the hemisphere contralateral to the blind field is absent or non-functional. Some can detect and localize simple targets and moving gratings, discriminate grating velocity, and differentiate forms in their blind field. It is opined that the subcortical pathways, primarily the superior colliculi, are involved in this process with the participation of the remaining hemisphere. Research has shown the existence of residual vision in the blind field; however, some persons after hemispherectomy are insensitive to motion-in-depth in their hemianopic field, while others possess blindsight as shown by a spatial summation effect i.e. subjects only react to the stimulus presented in their intact field, without being aware that the simultaneous presentation of another stimulus in their blind field lowers their reaction time. With this indirect method, blindsight could involve subcortical mechanisms without requiring cortical processing, and without the subject's awareness.

The superior colliculi are likely implicated in blindsight after hemispherectomy, researchers utilized the color vision properties of collicular cells to demonstrate its involvement in the residual visual abilities after hemispherectomy. Because the primate superior colliculi does not receive retinal input from shortwave-sensitive (S-) cones involved in color vision (consequently rendering them color blind to blue⁄ yellow stimuli) researchers tested three individuals after hemispherectomy who had reliably shown blindsight. A spatial summation effect only to achromatic stimuli suggested that their blindsight is color-blind to blue/yellow stimuli and does not receive input from retinal S-cone; therefore, researchers concluded that blindsight is likely mediated by the superior colliculus after genusogerecting.

Diffusion Tensor Imaging (DTI) Tractography was used to investigate pulvinar connectivity in humans and superior colliculi connectivity after hemispherectomy with and without blindsight. Researchers have demonstrated the presence of projections from the ipsi- and contralesional superior colliculi to primary visual areas, visual association areas, precentral areas/FEF and the internal capsule of the remaining hemisphere after hemispherectomy with 'Type I' or 'attention-blindsight' and an absence of these connections after hemispherectomy without it. In another study using fMRI, researchers demonstrated that, after hemispherectomy, achromatic stimuli but not S-cone-isolating stimuli in the blind field of a subject with blindsight activated visual areas FEF/ V5 and that the cortical activation pattern was enhanced by achromatic stimuli only. Researchers thus concluded that the human superior colliculi is blind to S-cone-isolating stimuli, and that blindsight is mediated by an S-cone-independent collicular pathway, at least in Hs.

The superior colliculi is the main recipient of retinal projections in lower mammals with a phylogenetically older and more primitive visual system than humans. Similar but weaker retino-collicular projections also exist in humans. Although existing superior colliculi connections to the remaining cortical areas seem to play a pivotal role in unconscious vision, blindsight subjects remain unaware of the information processed in their blind visual field. This may be due to a lack of synchronicity in cerebral activation. The human visual pathways process information simultaneously and yet are able to work independently of each other (as is the case following a circumscribed lesion in a visual cortical area). For conscious perception, however, a specific synchronized activation pattern of different cortical areas involving ventral, parietal and frontal visual areas is believed to be crucial. Our results indicate that individuals after hemispherectomy with 'Type I' or 'attention blindsight' are able to enhance visual performance in their blind field, but remain unaware of visual processing presumably because they are unable to access a more complex synchronous cortical activation pattern involving higher top-down mechanisms necessary for conscious vision.

B. TASTE, TEXTURE, AND SOUND

A particular concern of parent participants was the common occurrence of taste aversion, texture sensitivity, and sound sensitivity post-operatively. No parent had ever been warned that auditory processing would be a likely challenge post-operatively, yet most described that their child seemed to have at least some auditory processing issues. Similarly, many described texture aversion and difficulty eating or chewing. Several researchers expressed a desire to re-map the sensory homunculus post-hemispherectomy.

VI. BEHAVIOR AND EXECUTIVE FUNCTION

Behavioral problems, mood difficulties, and executive dysregulation, are possible consequence of hemidisconnection and are potentially key components in maximizing academic success, quality of life, and future independence. Understanding predictors of these difficulties is critical to the development of targeted behavioral interventions to improve functioning and quality of life after surgery.

Behavioral/mood and executive functioning are prevalent concerns for parents. One study shows that 71% of parents have significant concerns regarding behavior or mood, and 76% endorsing significant concern about executive function. Children with left hemisphere surgery were more likely to be described as "silly", "energetic", "happy" and "immature", whereas children with right hemisphere surgery were more likely to be described as "moody", "sad", or "irritable". Parents of children with left hemisphere surgery were more likely to endorse significant symptoms on the scales assessing hyperactivity, lack of inhibitory control, and overall executive function, while parents of children with right hemisphere surgery more often endorsed symptoms on scales measuring social withdrawal, somatic complaints, attention, ability to complete self-care activities independently, and working memory. It was discussed that these patterns of symptoms were not universally seen by side of surgery, and that rather than try to predict the patterns based on medical factors, it may be more important to identify common patterns of symptoms that can lead to more target interventions. Interestingly, health related quality of life (HRQOL) was significantly related to scores on both rating scales, with mood, behavior, and executive dysfunction all impacting social HRQOL, and behavior and executive dysfunction impacting school HRQOL.

VIII. MAPPING THE NETWORKS – FUNCTIONAL ORGANIZATION OF BRAIN NETWORKS IN CHILDREN AFTER HEMISPHERECTOMY

Recent advances in functional magnetic resonance imaging (fMRI) have enabled the study of spontaneous neural activity and brain network interactions at rest (e.g., data collected while subjects engage in a low-level task such as fixating on a central cross). Since the discovery that spontaneous fluctuations during rest were coherent within the somatomotor system, several researchers have confirmed that many of the networks known to be engaged during various cognitive tasks are also identifiable during resting states.

In one study which addressed the language networks in the intact hemisphere of children who have undergone left hemispherectomy, researchers qualitatively compare language networks with typical controls. Remarkably preserved patterns of functional connectivity were observed in the remaining hemisphere of these patients, suggesting possible dynamic reorganization capabilities in the developing brain. Specifically, functional connectivity of language areas in the right inferior frontal gyrus appears to be maintained with canonical language areas including angular gyrus, superior temporal gyrus, and premotor regions. This suggests that characterization of the functional integrity of right hemisphere language networks in children with left hemispherectomy may provide a means for predicting response to therapies post surgery.

VIII. COGNITION, LITERACY, AND LANGUAGE

Researchers agreed that there is a paucity of neurocognitive research dedicated to the study of children and adolescents who have undergone hemispherectomy; however, initial data shows that children who have undergone hemispherectomy often develop or recover near-normal language and literacy skills, yet the characteristics of these profiles are under-examined.

In one pilot study, cross-sectional investigation of reading and component skills considered building blocks of literacy development, children after left hemispherectomy were compared to two groups: otherwise typically-developing children with developmental dyslexia and typically developing readers. Children after left hemispherectomy only were selected because language processing tends to be left hemisphere dominant, thus informing the question *what is the maximum potential of the right hemisphere to support language and literacy development?* This is important to understand because dyslexics have been found to rely on the right hemisphere to read.

Healthy readers significantly outperformed both dyslexia and hemispherectomy groups. On nearly all tests children with dyslexia scored higher than the left hemispherectomy group. Initial findings indicate that children who have undergone hemispherectomy score in the low average to average range with highly variable vocabulary skills, relative strengths in timed word reading, with relative weaknesses in untimed word reading and comprehension. Surprisingly, pilot data also indicated that, on average, children after left cerebral hemispherectomy *outperformed* readers with dyslexia on timed word reading measures and showed a benefit (although not statistically significant) in timed over untimed reading conditions.

Although one might expect more pronounced interruption of language following a left hemisphere resection, the most significant differences in neurocognitive profiles were driven by functions that have been traditionally associated with hemisphere-specific functions (e.g., local vs. global processing). In one study addressing bilingualism in two individuals after hemispherectomy (one left, one right), qualitative analysis demonstrates that although scores are impaired on different tests, deficient approaches to particular tests were driven by deficits associated with the resected hemisphere “typical” functions. For example, while they both demonstrated impaired performances on a block design task, the participant after left hemispherectomy demonstrated better general meta-awareness for visual information (i.e., copying a complex figure and visual abstract reasoning) configurations but had difficulty integrating the details into the design. The participant after right hemispherectomy, on the other hand, had difficulty appreciating the overall contour of figures and her approach to these visual tasks was segmented and piecemeal.

Furthermore, this meta-awareness in the processing of visual information translated to verbally-mediated tasks. Namely, the performance of the subject after left on a task of verbal learning and memory of unstructured information represented a relative weakness for her in contrast to the relative strength of the right hemispherectomy subject on the same task. Once the verbal information was presented in a structured format, their scores were inverted such that the child after right hemispherectomy's performance declined once the scaffolding was provided for her.

Findings demonstrate that neuropsychological testing should be an integral aspect of the educational and treatment planning of children who have undergone hemispherectomy. That is, while gross measures of intelligence and verbal/non-verbal performance may indicate a certain level of functioning, detailed analysis of the strategies utilized by them to different tasks can shed light into cognitive rehabilitation strategies for each child by "playing to their strengths."

In future research, longitudinal studies charting the development of these skills as well as more general cognitive abilities is necessary to both compare developmental trajectories of reading and better understand mechanisms guiding these processes. In addition, researchers were encouraged to study the role of etiology and, therefore, nature and timing of initial insult related to reading and language outcomes.