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COMMENTARY:

Improving the Prognosis for Children with Autism Spectrum Disorders: A Comprehensive Developmental Approach to Intervention

**Stanley I. Greenspan, M.D. and
Ricki G. Robinson, M.D., M.P.H.**

New biomedical and clinical findings are improving the prognosis of many children with Autism Spectrum Disorders (ASD). As these findings help more children become able to engage in learning interactions, it is essential to offer them a comprehensive intervention program that works on reversing the core developmental deficits of ASD, as well as improving the symptoms.

Mounting research suggests that in children with ASD, fundamental developmental processes are disrupted. These include the capacity for shared or joint attention, reciprocal emotional and social interactions, including subtle affect gesturing, creative and meaningful use of language, and high levels of inferential reflective thinking including empathy and theory of mind (Dawson, Warrenburg, & Fuller, 1982; Just, Cherkassky, Keller, & Minshew, 2004; Minshew & Goldstein, 1998; Mundy, Sigman, & Kasari, 1990; Siller & Sigman, 2002). Furthermore, emerging evidence suggests that caregivers who work on these processes may help their children make more progress, especially in language and thinking capacities than caregivers who do not (Siller & Sigman, 2002).

In addition, disruption of these fundamental processes tends to lead to symptoms such as self absorption, self stimulation, perseveration, and scripted use of language.

There is also considerable evidence that genetic and biologically based developmental patterns are instrumental in disrupting these fundamental processes associated with healthy relating, thinking, and communicating (Anderson & Hoshiono, 1997; Bailey, et al., 1995; Bauman, 2000; Kemper & Bauman, 1998; Minshew, Sweeney, & Bauman, 1997; Piven, Arndt, Bailey, & Andressen, 1996; Sweeten, Posey, Shekhar, & McDougle, 2002).

Historically, it was believed that only surface behaviors and symptoms associated with ASD could be altered and that these fundamental developmental processes that

were disrupted due to biological differences were not very amenable to favorable change. A large number of studies on behavioral interventions focusing on changing surface behaviors and symptoms showed that it was possible to make modest gains in behavioral and educational outcomes. The most recent comprehensive study of intensive behavioral approaches (ABA – Discrete Trial), and the only clinical trial study done on behavioral approaches showed, however, that contrary to the original Lovaas' studies (Lovaas, 1987; McEachin, Smith, & Lovaas, 1993), educational and behavioral gains were quite modest and there were little to no differences shown in emotional and social functioning between the intervention group and the control group (Smith, Groen, & Wynn, 2000).

Newer relationship-based developmental approaches are demonstrating that it is possible to favorably influence the core developmental processes disrupted in ASD. These studies are showing, for example, that shared or joint attention, engagement, reciprocal emotional and social interactions can be significantly improved (Greenspan & Wieder, 1997, 1999; Greenspan, 2004).

In a recent report from the National Academy of Sciences, it was concluded that there was some evidence for both relationship-based and behavioral models and that interestingly, behavioral models were moving more towards incidental and spontaneous learning opportunities and therefore becoming more similar to the relationship-based approaches (Committee on Educational Interventions for Children with Autism, 2001).

There is also evidence for the value of working with individual processing differences in children with ASD, including auditory processing and language, motor planning and sequencing, sensory modulations (over- or under-reactivity), and visual spatial processing, e.g., occupational therapy, speech therapy, etc. There is also evidence that family support and work on family relationships is an important ingredient of a comprehensive program (Tsakiris, 2000).

One of the models cited in the Academy of Sciences Report is a comprehensive model that organizes the elements cited above in an integrated fashion that can be tailored to the needs, i.e., individual developmental profile of each child and family. This model, which is described as the Developmental, Individual Difference Relationship-Based Model (DIR[®]) (Also often referred to as Floortime), focuses on constructing an assessment and treatment program that works with all facets of the child's disorder and identifies and intervenes with the child and family's unique pattern. It has been shown that the DIR[®] Model works on both the core developmental processes necessary for a child to learn how to relate, communicate, and think as well as surface symptoms such as self-absorption, perseveration, and self-stimulation. A subgroup of children receiving this approach have been shown to master high levels of empathy, creative and reflective thinking, and social skills, including theory of mind, levels that in the past have been thought to be beyond the capacities of children with ASD. Other subgroups with greater degrees of initial impairments have also made more progress than formerly expected. They have been shown to become warm and loving, very interactive, and communicative, but have not achieved the same levels of language and thinking as the subgroup described above (Greenspan & Wieder, 1997, 1998, 1999; Tsakiris, 2000).

As new advances in understanding the biological pathways associated with ASD are emerging, a developmentally based intervention program, such as the DIR[®] Model, is especially important. New biological findings have the potential to improve prevention and biomedical management. Therefore, more children with ASD will have improved potential for learning to relate, communicate, and think. Yet the vast majority of these children may have already missed a number of their critical developmental foundations. These children require an opportunity to master these missed essential foundations for relating, thinking, and communicating rather than only working on surface behaviors and symptoms. In other words, the more effective the field's biomedical interventions, the more essential it is to offer an intervention program that works on the fundamental developmental processes necessary for healthy development because more children will have greater potential to master them.

In addition, a comprehensive developmental approach to assessment and evaluation as defined by the DIR[®] Model enables the field to improve the characterization of individual variation. Standard research validated approaches such as the ADI and ADOS can be used to establish the overall diagnoses of autism. However, emerging clinical observations are demonstrating that within the broad diagnosis of autism children vary considerably, on such dimensions as reactivity to sensation (some are very over-reactive and some quite under-reactive and this reactivity can vary from sensory modality to sensory modality), as well as motor planning and sequencing, visual spatial processing, auditory processing and language and their degree of engagement, two-way communication with gestures, and use of ideas. Therefore, it is essential to be able to subtype the children along these dimensions in order to have categories that may yield consistent biological findings. At present, it is highly likely that many different subtypes are being considered as one entity leading to difficulty in identifying a consistent biological pathway for ASD. Subtyping on the basis of biological patterns and observed clinical features together, rather than biological findings alone, will pave the way to improved understanding of emerging findings.

The DIR[®]-based clinical subtypes can also help the field interpret and translate evaluation findings into different treatment profiles within a broad comprehensive approach. In other words, subtyping will enhance the field's capacity to tailor the approach to the unique features of each child and family.

For a description of the DIR[®] model please see the following references by Greenspan & Wieder: the book entitled, *The child with special needs: Encouraging intellectual and emotional growth*, the article published in *J.A.S.H.: A functional developmental approach to autism spectrum disorders*—and the ICDL publications: *Clinical practice guidelines: Redefining the standards of care for infants, children, and families with special needs* and *The ICDL Training Videotapes on the DIR[®] Model and Floor Time Techniques*.

In conclusion, recent research is demonstrating that it is now possible to work on core deficits found in children with ASD in addition to surface symptoms and behaviors. Strategies to work on the core deficits that derail relating, communicating, and thinking is making it possible to tailor approaches to each child's unique profile and to help them master fundamental, emotional and intellectual developmental capacities and therefore improve their prognosis.

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GUIDING CHILDREN ON THE AUTISM SPECTRUM IN PEER PLAY:

Translating Theory and Research into Effective and Meaningful Practice

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Abstract: *Children on the autism spectrum encounter significant challenges learning how to play and socialize with peers. To help guide practitioners and family members in intervention efforts, this paper aims to translate theory and research into effective and meaningful practice focusing on the Integrated Play Groups (IPG) model. This multi-dimensional intervention specifically incorporates evidence-based practices that are pertinent to the development of social interaction, communication, play and imagination in children with ASD. The model's conceptual foundation is discussed in terms of representational and social play patterns and variations of children with ASD as well as developmental and socio-cultural perspectives on play's prominent role in childhood. Major features of the IPG model are presented followed by a case illustration of key practices for guiding peer play. The paper concludes with an overview of selected studies focused on the application of the IPG model and implications for future directions in research.*

Keywords: autism: autism spectrum, peer relations, play, inclusion

Max is a 7-year-old boy who was diagnosed with autism at the age of 4. Max has a limited repertoire of spontaneous play interests. He has a fascination with packaged and canned foods. He enjoys reading the labels on the packages, lining them up and sorting them by color and size. Max's spontaneous communication consists primarily of immediate and delayed echolalia in which he repeats words and phrases. He often mimics television commercials while gazing at photographs of commercial products. Max has been described as having a passive social play style. He rarely overtly initiates play with his peers and has a tendency to remain isolated in social situations. Max is beginning to show an interest in his peers. During free play he will watch and play beside other children, particularly when they engage in the few activities that are of interest to him.

INTRODUCTION

When children with diverse abilities are given free reign to play with one another, it is apparent who is thriving and who is at risk in their development. Children with autism spectrum disorders, like Max, are among those who are at greatest risk as they experience difficulties in both representational and social forms of play. A “lack of varied and imaginative or imitative play” and a “failure to develop peer relationships appropriate to developmental level” are considered hallmarks of autism spectrum disorders (ASD) (Charman and Baird, 2002, p. 289). Defining features of ASD are closely connected to characteristic impairments in the development of reciprocal social interaction, communication and imagination (American Psychiatric Association, 2000). Without appropriate intervention, children with ASD are likely to remain on the fringes of peers groups deprived of opportunities to experience an otherwise rich and meaningful play life.

The myriad problems children on the autism spectrum encounter in play present significant challenges to educators, therapists and family members seeking to help them. Until relatively recently, interventions specifically aimed at improving play (particularly peer play) in children with ASD have had a relatively small role in the literature (for a recent review, see Wolfberg & Schuler, in press). Williams (2003) recently reported that only 7% of 161 studies that make reference to play in autism actually explicitly focused on play. The majority of these studies merely touched upon play as a context of other more specific aims or in relation to other developmental phenomena and/or treatment goals. Nevertheless, recent advances both in our understanding of ASD and social inclusion have underscored the value of play and peer interaction in educational and therapeutic interventions. Following an extensive investigation, the National Research Council (2001) ranked the teaching of play skills with peers among the six types of interventions that should have priority in the design and delivery of effective educational programs for young children with ASD.

While a recent comprehensive review of intervention efforts yielded a wide range of promising practices to promote various aspects of play in children with ASD, these greatly varied with respect to theoretical orientations, methods and contexts (Wolfberg & Schuler, in press). Such conceptual as well as procedural disparities make it difficult to articulate a coherent approach to intervention to guide practitioners and parents in their efforts to support children with ASD in play (both with and without peers). For instance, practices that involve adult imposed modes of behavioral training are difficult to reconcile with more loosely structured approaches of a developmental variety. Nevertheless, there are some encouraging trends in which play interventions are blending approaches and evidence-based practices as opposed to strictly adhering to a particular paradigm or method (Boucher & Wolfberg, 2003). Many of the play interventions reviewed make reference to the inherent value of more naturalistic approaches to support children with ASD in play. Such interventions are increasingly being carried out in natural settings as well as incorporating typically developing peers and siblings. As reflected in the assessments

and methods being used, there also appears to be a growing appreciation of individual differences with respect to the child's developmental level, style of learning and intrinsic motivation.

To arrive at a broader conceptual foundation that can incorporate complementary perspectives, a closer understanding is needed of how to combine different layers and configurations of support that promote play in children with ASD. To provide children with ASD sufficient and contextually relevant support, all of the factors known to affect play (both from a developmental and socio-cultural perspective) must be carefully weighed and considered when designing a comprehensive peer play intervention.

The Integrated Play Groups (IPG) model was designed in an effort to apply our best current knowledge to develop a comprehensive intervention to support children on the autism spectrum in natural play experiences with typically developing peers and siblings (for a comprehensive overview, see Wolfberg, 2003). This multi-dimensional model draws on current theory, research and evidence-based practices, incorporating parameters pertinent to the development of social interaction, communication, play and imagination in children with ASD.

The IPG model complements and extends other noteworthy play-based intervention models that are grounded in child-centered practices. Of particular relevance for readers of this journal is the "Floor Time" approach developed by Greenspan and Wieder (1997ab) as a part of their comprehensive Developmental, Individual-Difference, Relationship-Based model (DIR[®]) Wieder & Greenspan, 2003). Although "Floor Time" differs from the IPG model with its emphasis on reciprocal play between an adult and child as opposed to adult guided peer play, there are a number of common threads. Both models focus on following the child's lead—as opposed to directing the child—to stimulate, expand and scaffold social interaction, communication and play along the lines of a progression that mirrors typical development. Each approach aims to build on the child's spontaneous initiations in play with objects, self and others guided by a careful appraisal of the child's developmental status across multiple domains (i.e., cognitive/symbolic, social, communicative, linguistic, sensory). Each approach similarly seeks to establish a joint focus in play routines and promote increasingly complex social-communicative exchanges through the use of rich affect, mutual imitation and drama.

To guide practitioners and family members in their efforts to support children with ASD in peer play, the present paper aims to translate theory and research into effective and meaningful practice with a focus on the IPG model. To establish a conceptual foundation, play patterns and variations of children with ASD will be highlighted while focusing on representational and social dimensions of play. A discussion of play's prominent role in childhood from developmental and social-cultural perspectives will further elucidate the need to support children with ASD in peer play. The IPG model will next be described followed by a case illustration of key practices for guiding peer play. The paper will conclude with an overview of selected research focused on the application of the IPG model.

Children on the Fringes of Peer Play

Play Patterns and Variations of Children on the Autism Spectrum

Although children on the autism spectrum naturally differ from one another in distinct ways, as a group they similarly face a number of challenges when it comes to play. A common misconception is that they are incapable of play and consciously choose to be isolated rather than in the company of peers. Yet there is ample clinical and research-based evidence to suggest that it is not simply a matter of lacking any drive or proclivity to play and socialize with peers—rather their play and social overtures are expressed in ways that are uniquely their own. Children with ASD indeed share many of the same desires and capacities for play, companionship and peer group acceptance as typically developing children (Bauminger & Kasari, 2000; Jordan, 2003; Wolfberg, 1999; Wolfberg et.al., 1999). Nevertheless, numerous obstacles prevent these children from gaining access to learning the necessary skills that would allow them to actualize their potential for play. Children with autism present distinct patterns of play that may be understood along symbolic/cognitive and social dimensions.

As compared to the play of typically developing children, which reflects a growing propensity toward rich imagination and social reciprocity, the play of children with ASD is markedly stark and detached. Without any direction, these children tend to spend excessive amounts of time pursuing repetitive activities apart from others (Frith, 1989; Wing, Gould, Yeates, & Brierly, 1977). Many children get stuck on one or a few activities, which they may literally repeat over and over. Some children are attracted to conventional toys, activities and themes that reflect the play preferences of younger children as well as age-mates. Others develop unique fascinations or pre-occupations that revolve around objects and unusual interests. What is missing across these activities is the systematic variations along a theme, thus making activities appear void of purpose.

Play involving the manipulation or sensory exploration of objects and/or space occurs in children on the autism spectrum at higher rates than other forms of representational play and is less diversified compared to children of a similar maturational age (Libby et. al., 1998; Sigman & Ungerer, 1984; Tilton & Ottinger, 1964). Children with ASD are less apt than developmentally matched peers to spontaneously engage in functional play and rarely produce pretend play (for reviews, see Jarrold, 2003; Jarrold, Boucher, & Smith, 1996; Williams, 2003). When children do show these capacities, the play is less diverse, flexible and variable than that of typical children. They are more likely to fixate on one or a few activities that they may repeatedly carry out over extended periods of time.

With respect to social play with peers, children with ASD encounter numerous barriers that are difficult to overcome (for reviews see Jordan, 2003; Williams, Costell & Reddy., 1999; Wolfberg, 1999; 2003). Overall, they direct fewer obvious social initiations to peers as well as inconsistently respond to peers when they initiate with them. When children with ASD do make attempts to interact with peers, their initi-

ations have a tendency to be subtle, obscure or poorly timed (Lord, 1984; Lord & Magill, 1989). Problems in verbal as well as non-verbal forms of social communication (e.g., the use of eye gaze, eye contact, physical proximity, facial expression, proto-declarative pointing and other conventional gestures) closely interface with underlying difficulties in joint attention, spontaneous imitation and emotional responsiveness in social play (Baron-Cohen, 1989a; 1989b; Dawson & Adams, 1984; Lewy & Dawson, 1992; Mundy et al., 1986; 1987; Sigman & Ruskin, 1999; Wetherby & Prutting, 1984).

Based on clinical observations, children with ASD present distinct social play styles that are consistent with Wing and Gould's (1979) early work. Some appear more "aloof" than others as they may distance themselves from peers or act as though they are unaware of their presence. Others tend to be more "passive" as they may follow along or watch what their peers are doing, but rarely initiate interaction in obvious ways. Still others are "active and odd" in the sense that they may indeed attempt to engage peers, but do so in an idiosyncratic or one-sided manner such as by talking excessively about one topic.

Play's Prominent Role in Childhood

Developmental and Socio-Cultural Perspectives

Looking at play's prominent role in childhood, both from a developmental and socio-cultural perspective, gives further insight into addressing children's competence in both representational and social play. Vygotsky (1966; 1978) ascribed a most vital role to play as a prime social activity through which children develop symbolic capacities, interpersonal skills, and social knowledge. In his writings he noted that play's significance extends beyond that of representing stages of development to that of actually leading development. He further emphasized the notion that all learning and development is mediated through social experiences with adults and peers.

When it comes to play, peers in particular perform a distinct role in supporting development that is essentially impossible for adults to duplicate (Hartup 1979, 1983; Wolfberg et al., 1999). The extent to which children may gain access to and garner the advantages that play experiences have to offer is largely influenced by the peer group or peer culture (Corsaro, 1992; Wolfberg et al., 1999). Ultimately, it is through active participation in the play culture (defined as the unique social and imaginary worlds that children create together apart from adults) that children construct shared meanings, and transform their understanding of the skills, values, and knowledge inherent to society and culture at large (Mouritsen, 1996; Selmer-Olson, 1993; Wolfberg, 1994;1999).

For many children with ASD the reality is that they are often excluded from their peer culture. The unusual ways in which they respond and relate to objects and people often sets these children apart from their peer group. Unconventional attempts to play and interact are commonly perceived by peers as signs of deviance, limited

social interest, or even rejection. As a result, many children with autism become targets of bullying, teasing and taunting by intolerant peers (Heinrichs, 2003) while others are simply ignored or overlooked by more tolerant and benevolent peers (Wolfberg et.al, 1999). Consequently, many children with ASD become caught in a cycle of exclusion, which deprives them of opportunities to learn how to socialize and play in more conventional and socially accepted ways.

Understanding play's role from this perspective not only has profound implications for our understanding of the problems children with ASD encounter, but also provides compelling evidence for the importance of peer play interventions. In order to break this cycle of social exclusion, intervention efforts would need to carefully consider the role of the peer culture as it interfaces with the child's overall development and socio-cultural experience within the context of play.

Guiding Peer Play

Integrated Play Groups (IPG) Model

The IPG model is explicitly designed to support children on the autism spectrum (novice players) in mutually enjoyed play experiences with typical peers/siblings as playmates (expert players). Infusing a Vygotskian perspective, the IPG model features "guided participation" in play, described as the process by which children develop through active participation in culturally valued activity with the guidance, support and challenge of companions who vary in skill and status (Rogoff, 1990). Through a carefully tailored system of support, the intervention seeks to maximize each child's developmental potential as well as intrinsic desire to play, socialize and form meaningful relationships with peers. An equally important focus is on teaching the peer group to be more socially responsive to and accepting of children with different ways of playing, communicating and relating.

Program and Environmental Features

IPGs are customized for children (ages 3 to 11 years) as a part of an individualized educational or therapeutic program. Play groups are facilitated by a trained adult referred to as a play guide. Each group is made up of a consistent group of three to five children with a higher proportion of expert (typical peers and/or siblings) to novice players (children with ASD). Expert players are recruited from places where children ordinarily have contact with peers (e.g., school, family friends, neighbors, community). Playmates ideally have some familiarity and attraction to one another and the potential for developing long-lasting friendships. Groups may vary with respect to children's gender, ages, developmental status and play interaction styles offering different types of beneficial experiences.

IPGs take place in natural play environments within school, home, therapy or community settings (e.g., inclusive classrooms, after-school programs, recreation centers or neighborhood parks). Play groups generally meet twice a week for 30-to-60 minute sessions over a 6-to-12 month period. Times may vary depending upon the age and developmental stage of the participating children.

Play spaces are specially designed based on a consideration of multiple factors including size, density, organization and thematic arrangements. Play materials include a wide range of highly motivating sensory motor, exploratory, constructive and socio-dramatic props with high potential for interactive and imaginative play. Play materials vary in degree of structure and complexity to accommodate children's diverse interests, learning styles and developmental levels.

Play sessions are structured by establishing consistent schedules, routines and rituals and incorporating visual supports that foster familiarity, predictability and a cohesive group identity. Personalized visual calendars and schedules help children anticipate the days and times of meetings. Basic rules for fair and courteous behavior and appropriate care of materials are presented at the outset of play groups. Play sessions begin and end with an opening and closing ritual (e.g., greeting, song and brief discussion of plans and strategies). Group membership is established by creating play group names and associated rituals.

Corresponding to the robust visual-spatial strengths characteristic of the cognitive and processing styles of children with ASD, visual supports are customized for individual children (Wolfberg & Tuchel, submitted for publication). Varying in form and function, visual supports (including Augmentative and Alternative Communication strategies) that range from concrete to abstract and include the use of tangible symbols, line drawings, photographs and/or written words to guide children in social play experiences (see for example, The Picture Communication Symbols ©1981-2002 developed by Mayer-Johnson, Inc., and adopted for use by TEACCH (Schopler & Mesibov, 1986) and PECS (Frost & Bondy, 1994). Examples of visual supports include: play area organizers, schedules, play group rules, play session sequence, choice board of preferred play activities, personalized play group posters, social-communication cues, role tags, play props, play theme books.

Assessment Approach

Play guides are well versed in the range of assessment tools and techniques specifically developed for use with this model (Wolfberg, 2003). Systematic observations provide a basis for setting realistic and meaningful goals, guiding intervention strategies, and systematically documenting and analyzing the children's progress. Assessments include a focus on symbolic and social dimensions of play, communicative functions and means, play preferences and diversity of play.

Symbolic/cognitive dimensions of play refer to play acts that the child directs toward objects, self, or others and that signify events (adapted from McCune-Nicholich 1981; Piaget, 1962; and Smilansky 1968). These include exploratory play

(manipulation), conventional object use and simple pretense (functional), and advanced pretense (symbolic/pretend). Social dimensions of play focus on the child's distance to and involvement with one or more children (adapted from Parten, 1932). These include playing alone (isolate), watching peers (onlooker/orientation), playing beside peers (parallel/proximity), playing with peers in joint activity (common focus), and collaborating with peers in an organized fashion (common goal). Although each set of play characteristics appears to follow a relatively consistent developmental sequence, they are not considered mutually exclusive stages of development.

Communicative functions describe what the child communicates within the context of peer play activities (e.g., requests for objects or peer interaction, protests, declarations, and comments). The functions of communication may be accomplished through a variety of verbal and non-verbal communicative means (e.g., facial expressions, eye gaze, proximity, manipulating another's hand, face, or body, showing or giving objects, gaze shift, gestures, intonation, vocalization, non-focused or focused echolalia, and one-word or complex speech/sign)(adapted from Peck, Schuler, Tomlinson, Theimer, & Haring, 1984).

Documenting the play preferences of both novice and expert players in play groups offers a means in which to identify and match children's play interests. Play preferences include a child's attraction to toys or props (e.g., prefers round objects, toys that move, realistic replicas), interactions with toys or props (e.g., prefers to spin toys, line up toys, conventional object use), choice of play activities (e.g., prefers rough-housing, quiet play, constructive play), choice of play themes (e.g., prefers familiar routines, invented stories, fantasy play), and choice of playmates (prefers no one in particular, one or more peers). Documenting the play preferences of the children with ASD further provides a means to assess diversity of play.

Intervention Practices

The intervention, "guided participation" involves a carefully tailored system of support that is responsive to each child's unique profile of development and socio-cultural experience while also sufficiently intensive to maximize the child's potential. The overall premise is to allow novice and expert players to initiate and incorporate desired activity into socially coordinated play while challenging novice players to practice new and increasingly complex forms of play. To achieve this, the adult guides novice and expert players to engage in mutually enjoyed play activities that encourage social interaction, communication, play and imagination – such as pretending, constructing, art, music, movement and interactive games. Gradually the adult support is decreased as the children learn to mediate their own play activities. To guide peer play, the following key set of practices are applied:

Monitoring play initiations. This practice involves recognizing, interpreting and responding to the novice player's spontaneous attempts to socialize and play. Play initiations may include virtually any act or display that indicates a child's interest or desire to play in the company of peers. They may be directed to objects (e.g., toys

and props), others (e.g., peers and adults) or oneself. Play initiations may be conventional or unconventional in nature and conveyed through overt, subtle or obscure means. Even acts that reflect unusual fascinations, obsessions, rituals or idiosyncratic language are recognized as play initiations. Play initiations are the foundation on which to build upon the child's social and symbolic play repertoire. They are the springboards for novice and expert players to find common ground in mutually engaging activities. The adult's capacity to recognize, interpret and respond to play initiations is essential for delivering support that is matched to the level of comprehension and ability within the child's "zone of proximal development" (Vygotsky, 1966; 1978).

Scaffolding play. This practice involves building on the child's play initiations by systematically adjusting assistance to match or slightly exceed the level at which the child is independently able to engage in play with peers within the child's "zone of proximal development." Scaffolding is a fluid process that relies entirely upon the adult's ability to respond to all of the players' interests, abilities and needs at any given point in time. The idea is to avoid being either too lax or overly intrusive. The key is to find that ever so delicate balance of knowing when to step in, when to step out and especially when to be quiet while sustaining child engagement. At a more intensive level, the adult directs the play event and models behavior much like the director of a stage performance by identifying and/or narrating common themes, arranging props and assigning roles and play partners. At a less intensive level, the adult guides the children to set the stage for their own play by posing leading questions, commenting on activities, offering suggestions and giving subtle reminders using verbal and visual cues. As the children grow increasingly comfortable and competent in their play, the support is withdrawn. Eventually, the adult remains on the periphery of the group offering the children a "secure base" from which to explore and try out new activities.

Social-communication guidance. This practice supports novice and expert players in adopting the use of conventional verbal and nonverbal strategies to elicit one another's attention and sustain mutual engagement in play. Directed to novice and expert players alike, these strategies are presented in the form of social-communication cues. Social-communication cues focus on what the players may do and/or say to invite and join peers for play. Specifically, strategies focus on (a) initiating play with peers (including persisting in enlisting reluctant peers), (b) responding to peer social bids, (c) joining or entering established play events with peers, and (c) maintaining and expanding reciprocal exchanges in play with peers. Relevant cues are selected based on observation and analysis. The cues are then introduced and reinforced with the aid of visual supports. The intent is for children to naturally incorporate these strategies into their repertoire, and to no longer rely on adult guidance or the presence of visual cues.

Play guidance encompasses a set of strategies that support novice players in peer play experiences that are slightly beyond the child's capacity while fully immersed in the whole play experience at his or her present level, even if participation is minimal. Play guidance strategies range from orienting (watching peers and activities),

imitation and mirroring (mimicking the actions of a peer), parallel play (playing side by side in the same play space with similar materials), and joint focus (active sharing and informal turn-taking in the same activity) to socially coordinated activity involving joint action (formal turn-taking), role enactment (portraying real life activities through conventional actions), and role playing (taking on pretend roles and creatively using objects while enacting complex scripts). As represented in the following case illustration, novices may carry out play activities and roles that they may not as yet fully comprehend. By building upon play initiations, and encouraging participation in activities that are just slightly beyond the child's present abilities, novices may begin to explore and diversify existing play routines.

Case Illustration of an Integrated Play Group

The following case illustration of Max appears in Wolfberg (2003, p. 206-208) Max attends a special day class in a public elementary school. He participates in Integrated Play Groups with one other novice player from his class and three expert players from a third-grade general education class. His teacher is the play guide. The groups meet twice a week for 30 minutes in the afternoon.

Based on a thorough assessment, the focus of the intervention is on extending Max's development in the following areas: (a) representational play (i.e., functional play) by enacting simple scripts around familiar routines with realistic props, (b) social play by establishing a common focus with peers, (c) social-communicative competence by increasing the rate of spontaneous initiations (using more effective verbal and nonverbal means) and (d) expanding and diversifying his repertoire of play interests.

Play Scenario	Monitoring Play Initiations	Scaffolding Play	Social-Communication Guidance	Play Guidance
<p>The session opens with a ritual greeting and a recap of the last session. The teacher asks the children to think of things they would like to play together.</p> <p>Max heads directly to the play grocery store and begins lining up tins on the shelf, reading aloud each package label. Ricky and Ute (expert players) gravitate to the grocery store and stand behind the cash register. Lisa and Nina (novice and expert players) say they would like to play dolls</p>	Recognize play initiation	Intermediate Support—Verbal and Visual Cueing		

Play Scenario	Monitoring Play Initiations	Scaffolding Play	Social-Communication Guidance	Play Guidance
<p>The teacher suggests that Lisa and Nina go shopping with their babies while Max, Ute and Ricky work together in the store.</p> <p>Pointing to the picture cue, the teacher says, “Max and Ricky, why don’t you take turns stocking the grocery shelves and stamping imaginary price labels on each item.”</p>	<p>Interpret and respond to play initiation Visual Cueing</p>	<p>Intermediate Support – Verbal and</p>	<p>Reinforce cue – What to Do – “take turns”</p>	<p>Joint Action / Role Enactment</p>
<p>Together the boys line up tins, boxes and play food on the shelves. Using a plastic tube, Ricky pretends to stamp labels on some of the items, “Okay, 95 cents for Cocoa Puffs, 75 cents for Campbells soup, 25 cents for spaghetti.”</p>		<p>Minimum Support – Standing By</p>		<p>Joint Action/ Role Enactment</p>
<p>Pointing to a poster with a corresponding cue, the teacher tells Max to watch what Ricky is doing.</p> <p>Max watches. Ricky next hands him a plastic tube and shows him how to “stamp” the rest of the items. Max takes the plastic tube and imitates the action by stamping several new items and saying, “Cheerios, 25 cents, Rice-a-roni, 25 cents, Fritos corn chips, 25 cents</p>		<p>Intermediate Support – Verbal and Visual Cueing</p> <p>Minimum Support – Standing By</p>	<p>Reinforces cue – What to Do – “watch”</p>	<p>Joint Action / Role Enactment</p>
<p>Meanwhile, Lisa and Nina begin loading a shopping cart with grocery items. Ute offers Max the role of bag boy while she runs the cash register. Max follows Ute and stands beside the cash register. Ute hands Max a paper bag and shows him how to hold it open. Max waits for further direction.</p> <p>The teacher steps in and demonstrates each step of the check-out sequence. She suggests that Ute say “take” to Max, each time she gives him an item to put in the bag.</p>	<p>Recognize play initiation</p> <p>Interpret and respond to play initiation</p>	<p>Minimum Support – Standing By</p> <p>Maximum Support – Directing and Modeling</p>	<p>Reinforce cue – What to Do – “take”</p>	<p>Joint Action / Role Enactment</p>

Play Scenario	Monitoring Play Initiations	Scaffolding Play	Social-Communication Guidance	Play Guidance
<p>The children establish a rhythm. Lisa and Nina take turns unloading the shopping cart one item at a time – Ute rings up each item on the cash register and hands the item to Max – Max puts each item in the grocery bag.</p> <p>When they finish checking out, Ute tells the shoppers, “Thank you for shopping at Lucky supermarket, have a nice day” The shoppers say, “Thank you, bye-bye.”</p>		Minimum Support – Standing By		Joint Action / Role Enactment
<p>The teacher probes, “What should the bag boy say?” Ute tells Max to say, “Thank you, bye-bye, have a nice day,” which Max repeats with a beaming smile.</p>		Intermediate Support – Verbal Cueing	Introduce Cue – What to Say – “Thank you ...”	Role Enactment

Efficacy of the IPG Model

Research Highlights

To evaluate the efficacy of the IPG model, a series of experimental and exploratory studies have been carried out (for a detailed overview, see Wolfberg, 2003 – Appendix B). Much of our research has focused on documenting the effect of the intervention on the novice players’ development of representational and social play as well as the possible influences that shaped their experiences (O’Connor, 1999; Wolfberg, 1988; 1994; 1999; Wolfberg & Schuler, 1992; 1993; Yang, et al, 2003; Zercher et al., 2001). The accumulated findings provide consistent evidence that the children with ASD spontaneously generated more diverse and complex forms of play along cognitive/symbolic and social dimensions than previously exhibited in unsupported peer play activity. Moreover, the children maintained these skills when adult support was withdrawn. Specifically, the children exhibited: (1) decreases in isolate and stereotyped play, (2) increases in interactive and reciprocal social play with peers (parallel, common focus/goals), (3) increases in representational forms of play (i.e., functional, symbolic/pretend). Improvements in language were also documented in a few cases. Further, observational and social validation data indicated that the children’s advances in play generalized beyond the specific play group to other peers and siblings, settings (school, home, community), and social activity contexts.

In addition to evaluating outcomes for novice players’, we also examined

changes in expert players' attitudes, perceptions, knowledge and experience while participating in the IPG intervention (Gonsier-Gerdin, 1993; Wolfberg, 1994/1999; Yang et al., 2003). The data suggest that peers developed greater sensitivity, tolerance and acceptance of the novice players' individual differences. In addition, they articulated a sense of responsibility as well as an understanding of how to include the less skilled players by adapting to their different interests and styles of communication. They further reported having fun and developing mutual friendships with novice players that extended beyond the play group setting to after-school activities in the home and community.

There is also emerging evidence to suggest that expert players' social play interaction styles may possibly afford novice players different degrees of structure and support. Expert players with more dominant or authoritarian styles seemed to add a higher degree of structure and predictability to play scenarios. Peers who playfully teased and clowned around were seen as highly engaging as well as adding a dimension of flexibility. The nurturing, doting types tended to be patient as well as persistent while guiding the novice players in a manner consistent with scaffolding. Also of noted interest is that the play guides (teachers and therapists) reported that they themselves had benefited as facilitators of Integrated Play Groups and that the experience had an impact on their own understanding of and practice with children (O'Connor, 1999; Wolfberg & Schuler, 1992).

While it is not feasible to determine which components of the intervention were most pertinent to the observed changes since the IPG model specifically incorporates a selection of evidence-based practices, the cumulative findings suggest that the IPG model as a whole yielded generalized and socially valued gains. General findings and hypotheses educed from the accumulated data suggest that the system of support involving explicit guidance and peer mediation contributed to the children's social and symbolic growth. Immersion in mutually enjoyed play activity with more competent peers enabled novice players to polish their imitation skills and practice more advanced forms of social, communication and play.

It is important to point out that the collected studies reported here are limited in that they focus on a relatively small number of children who participated in the IPG intervention. In future research, it would be pertinent to carry out larger scale replications. In doing so, there are a number of questions that warrant further investigation through multiple modes of quantitative and qualitative inquiry. Future investigations are needed to further our understanding of which configurations of support best facilitate social and representational forms of play in children with ASD so that they may more fully participate in their peer culture. For instance, to what extent are specific play activities conducive to stimulating joint attention, imitation and social reciprocity with peers? How do such activities possibly correspond to children's specific social play styles? Questions concerning the interdependence of socially mediated support, children's play culture, and various domains of social and symbolic growth would also be pertinent to explore. The extent to which such guided peer play experiences contribute to long term peer relationships, particularly friendships, would be especially important to establish. Illuminating these interrelation-

ships would not only enhance our understanding of play development in children with ASD, but also how best to design effective and socially and culturally meaningful interventions.

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Extending Our Understanding of Bipolar Patterns in Children: Applying a Developmentally-Based, Individual Difference, Relationship-Based (DIR[®]) Model to Pediatric-Bipolar Disorder

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Abstract: *Bipolar disorder in children has been a highly controversial diagnosis. This paper describes bipolar patterns in children using a biopsychosocial developmentally based, individual difference, relationship-based model. After presenting a “bipolar signature,” a pilot study is described that investigated sensory processing and sensory modulation challenges in young children who met criteria for bipolar disorder. Children with bipolar patterns were found to have sensory and modulation challenges, particularly a pattern of atypical vestibular functioning.*

The history of bipolar disorder focuses on the development of the “concept” of bipolar disorder in adults. Until recently, research on bipolar disorder also focused on adults. Within the last twenty years we have begun to acknowledge that some patterns of severe emotional dysregulation in young children may be variants of the bipolar patterns that are seen in adults. However, we have not yet used a “developmental lens” to study these patterns in children; we do not have a developmental perspective for bipolar disorder. This paper looks at bipolar patterns using a biopsychosocial developmentally-based, individual difference, relationship-based model (DIR[®]). In addition, children who evidence bipolar patterns appear to have sensory processing and modulation problems that contribute to their aberrant emotional and social patterns. A pilot study investigating sensory processing and modulation is described that represents a first attempt to study sensory functioning in children with bipolar patterns.

Background

Pediatric bipolar disorder has been a highly controversial diagnosis. At the present time we are experiencing a controversy that is reminiscent of the reluctance to accept the diagnosis of depression in children before the 1970s. At that time it was felt that children did not have the psychological structures necessary to experience depression and therefore such a diagnosis was inappropriate in children. Bipolar disorder has experienced a similar course. For example, Charles Bradley, a prominent psychiatrist in the 1940s, wrote:

In children, sustained elevation of mood and exhilaration are not encountered except in response to reasonably appropriate stimuli....It is likely that in the rare reported cases of manic psychoses in children there may well have been confusion either in observation or interpretation of motor activity, impulsiveness, or other similar childhood symptoms, and attempts to fit the patient into an adult psychiatric classification which *does not apply to children* [italics supplied] seems unwarranted.... For the present it is best to avoid the diagnosis of manic-depressive psychosis or affective psychosis in children (Bradley, 1945).

Almost two decades later, Anthony and Scott (1960) developed a set of criteria that were almost impossible for children to meet for the diagnosis of manic-depression and essentially “killed” the diagnosis. It was “revived” with the work of Robert DeLong in the 1980s (DeLong, 1990). Weller et al (1986; 1995) were then highly influential in showing that pediatric bipolar disorder was both under-diagnosed and mis-diagnosed. During the 1990s and early 2000s, researchers have attempted to operationalize the concept of childhood bipolar disorder and to differentiate the disorder from adult-onset bipolar disorder.

However, for a child to be diagnosed with bipolar he or she must currently still meet adult criteria for a Manic Episode. Mania is defined in DSM-IV-TR “by a distinct period during which there is an *abnormally and persistently elevated, expansive, or irritable mood* (my italics). The *period* of abnormal mood *must* last at least a week (or less if hospitalization is required, Criterion A).” In addition to evidencing the cardinal symptoms of elevated mood and expansiveness or irritability and the duration criteria of one week, the disturbance in mood “must be accompanied by at least three additional symptoms that includes inflated self-esteem or grandiosity, decreased need for sleep, pressure of speech, flight of ideas, distractibility, increased involvement in goal directed activities or psychomotor agitation, and excessive involvement in pleasurable activities with a high potential for painful consequences. If the mood is irritable (rather than elevated or expansive), at least four of the above symptoms must be present (Criterion B).” Additional criteria include *not* meeting criterion for a Mixed Episode in which both a Manic Episode and a Depressive Episode occur nearly every day for at least a one-week period, experiencing a sufficiently severe disturbance that is marked by impairment in social or occupational functioning, requires hospitalization, or includes psychotic features, *not* being due to drug abuse, medication, or somatic treatments for depression, and *not* being due to the direct effects of a general medical condition (DSM-IV-TR, 2000).

In a research roundtable meeting at the National Institute for Mental Health on April 27, 2000, experts in the field of prepubertal bipolar disorder discussed a number of the controversial issues in the area of diagnosing bipolar disorder in young children. They concluded that a symptom pattern similar to adult-onset bipolar disorder with discrete episodes and clear onset and offset was not common in children. Rather, the most frequent presentation of the disorder in prepubertal children was characterized by “a long-duration episode with rapid cycling (ultradian or continuous cycling as the predominant type) and mixed mania (i.e., co-occurring mania and depression) (*Journal of the American Academy of Child and Adolescent Psychiatry*, 2001).” This pattern of behavior has been given the diagnosis “Bipolar Disorder-Not Otherwise Specified” (BP-NOS).

Leibenluft et al. (2003) have proposed a detailed classification of clinical phenotypes of juvenile mania based on three distinguishing features of the illness: (a) the duration of manic cycling; (b) the predominant mood state, i.e., predominantly euphoric/grandiose, or only irritable; (c) the presence of chronic dysphoria and anger dyscontrol. Staton et al (2004) proposed other criteria for differentiating bipolar children that included: (a) the amount of clinically significant depression; (b) the presence or absence of aggressive/violent rage; (c) the presence or absence of clinically significant distractibility; and (d) the predominant pattern of mood illness cycling.

While opening the door for discussion and research on bipolar disorder in children we are just beginning to tackle the problem of operationalizing the criteria for the disorder. The difficulty in doing so was underscored in 2003 when 22 experts in childhood bipolar disorder rated case material of children with moderate to severe mood instability. There was a high level of agreement on three cases with “narrow phenotype,” or classical bipolar patterns proposed by Leibenluft and her colleagues. However, there was poor agreement on diagnosis for children who evidenced more variable patterns including (a) DSM-IV criteria for mania but episodes that are shorter than four days; (b) DSM-IV criteria but with one too few of the “B” criteria (listed above); (c) irritability, sufficient “B” criteria, but no discernible episodes; and (d) children whose parent-observed mania was not observed elsewhere (Carlson et al., 2004).

A Developmental, Individual Difference, Relationship Based Model (DIR[®])

Recently, Greenspan and Glovinsky (2003) have explored bipolar patterns in children by using a Developmental, Individual-Difference, Relationship Based (DIR[®]) Model. This comprehensive framework is a multi-dimensional model that involves developmental, biological, psychological, and social factors and considers how three dynamic influences interrelate to guide development. These influences include: (a) the child’s biology and genetics; (b) family, environmental, and cultural factors that are woven into the parents interactions with their children; and (c) the

co-regulated affectively based interactions between the child and his/her caregivers. These influences interrelate and determine the child's capacity to master core functional emotional abilities that include the ability (a) to organize a calm and regulated emotional state and attend to multisensory affective stimuli; (b) to engage pleasurably with caregivers; (c) to initiate and interact in two-way co-regulated presymbolic gestural affective exchanges; (d) to extend these preverbal presymbolic exchanges into longer two-way co-regulated affective signaling and problem-solving communications that are sustained over time and space; (e) to begin to create and use ideas meaningfully and imaginatively, and to incorporate these ideas into symbolic play; (f) to build bridges between ideas that are the foundation for higher level logical and reality oriented thinking; and (g) to expand thinking capacities so as to include reflection, recognition of multiple causes to explain an event or behavior, and more differentiated (gray area) thinking, as well as an internal sense of self and inner standards. Greenspan has described three core components of the DIR[®] Model in a number of publications (Greenspan, 1992; Greenspan, 1997; Greenspan & Wieder, 1999; Greenspan & Glovinsky, 2003; Greenspan & Shanker, 2004).

The clinical work with children who have been diagnosed with bipolar disorder has suggested that these children constitute a unique pattern of Regulatory Disorder not identified under the current nomenclature of Diagnostic Classification:0-3 which includes four subtypes of Regulatory Disorders: (a) Hypersensitive, (b) Under-reactive, (c) Motorically Disorganized, Impulsive, (d) Other. A Regulatory Disorder is defined by **“both** a distinct behavioral pattern **and** a sensory, sensory-motor, or organizational processing difficulty (DC: 0-3, 1999). Greenspan & Glovinsky (2003) presented a novel hypothesis that had not previously been considered by other investigators attempting to operationalize the concept of childhood bipolar disorder. This hypothesis was based on early antecedents in sensory and motor functioning that affect parent/child interactions and subsequent emotional and behavioral development, and organization of a child's experience of self with others. Greenspan & Glovinsky (2003) hypothesized a “bipolar signature” in children at risk for bipolar mood dysregulation that included:

A unique pattern of sensory processing in which children respond to sensory oversensitivity with a paradoxical response. Whereas children in Type I Regulatory Disorders (Hypersensitive) respond to sensory overload by evidencing anxious, fearful, and cautious behavior, the bipolar child responds to sensory overload with increased behavioral activation, more sensory craving, particularly with regard to movement, and high activity, high agitation, and increased impulsivity. The more caregivers try to intervene, the more overloaded the child feels, increasing the behavioral activation rather than reducing it.

1. Furthermore, caregiver/child interactions are derailed, interfering with the development of fully co-regulated reciprocal affective exchanges. The rhythm, tempo, and pace of caregiver/child interactions are disrupted by severe emotional dysregulation. The normal capacities to “down-regulate” when the child is over-activated, or “up-regulate” when the child is in an “under-activated” mood state are dysregulated.

2. The consequence of chronic emotional dysregulation is the failure of the child to master higher functional emotional capacities of symbolizing ideas and affects. These children remain in a prerepresentational, somatic, or action mode, or their affects and emotions are represented as separate affect states that are polarized rather than integrated (Greenspan, personal communication, 2003).

Pilot Study

We have begun to explore these hypotheses using the Sensory Profile developed by Winnie Dunn (Dunn, 1999). This tool is a questionnaire “that measures a child’s processing abilities and the effect of sensory processing on the child’s functional performances in the child’s daily life activities” (Dunn, 1999). The series of profiles that now extends from infancy through adolescence consists of questions regarding Sensory Processing, Modulation, and Emotional Responses. In the specific version of the questionnaire used in our pilot study, the Sensory section assesses the child’s responses to auditory, visual, vestibular, touch, multisensory, and oral sensory processing. The Modulation section evaluates the child’s ability to regulate neurological messages by either facilitating or inhibiting different types of responses. Finally, the Behavioral and Emotional Responses section evaluates the child’s behavioral outcomes of sensory processing.

Our work on children at risk for bipolar disorder extends the Sensory Profile into an area not previously studied. The questionnaire has been used on a sample of children without disabilities and two samples of children with disabilities, including ADHD and autistic spectrum disorder.

METHODS

Parents were asked to rate their child on each of 125 items. The rating scale included the categories “Always, Frequently, Occasionally, Seldom, and Never.” The scores for six sensory areas, five modulation areas, and three emotional and behavioral outcome areas were compiled for 21 children ages three to ten years who had family histories of bipolar disorder dating back three generations, and who were referred for severe emotional dysregulation that in most cases precluded participation in traditional school programs. These children evidenced severe aggression, destructive behaviors, hyperactivity, severe tantrums, irritability, and sleep disturbances among their symptoms. Families were interviewed extensively by a psychologist and a psychiatrist, and parents filled out questionnaires that documented family, developmental, and behavioral histories. The parents and children were also videotaped in unstructured play sessions that were scored using the Functional Emotional Assessment Scale (FEAS) (Greenspan, DeGangi, & Wieder, 2001).

Scores for each child were transferred to a summary sheet that enabled researchers to compare the child's score versus scores for "Typical Performance, Probable Difference, and Definite Difference."

RESULTS

Our model predicted that children with bipolar patterns of mood dysregulation would evidence sensory processing challenges, including sensory over-reactivity and emotional reactivity. In addition we predicted that children would evidence vestibular processing challenges relating to regulating movement (under-reactivity and craving movement stimulation). In a large percentage of referrals for children who are subsequently diagnosed with bipolar disorder, parents are initially concerned about their highly activated behavior patterns. Many of these children are initially diagnosed with Attention Deficit Hyperactivity Disorder (Faedda et al., in press). Information from the vestibular system contributes to regulation of muscle tone and coordination, balance and equilibrium, ocular-motor control, the ability to maintain and transition between states of sleep and alertness, the level of attention, and emotional state (Williamson and Anzalone, 2001). Table 1 presents the means and standard deviations for the 21 children that comprised the present sample. The mean scores and standard deviations for each section and for each factor were then plotted into appropriate classification columns (Typical performance, Probable Difference, Definite Difference).

The results of this pilot study found that children with bipolar patterns obtained Definite Difference scores in Vestibular Processing, Emotional/Social Response, Behavioral Outcomes of Sensory Processing, and on the following Factors: (1) Sensory seeking, (2) Emotional reactivity, (4) Oral Sensory Sensitivity, and (5) Sensory Sensitivity. They also obtained Sensory Processing Probable Difference Scores in Auditory Processing, Touch Processing, Multisensory Processing, and Oral Sensory Processing. In the area of Modulation, they obtained Probable Difference Scores in Modulation Related to Body Position and Movement, Modulation of Movement affecting Activity Level, and Modulation of Visual input Affecting Emotional Response and Activity Level. They also obtained Probable Difference Scores on two Factors; (4) Oral Sensory Sensitivity and (9) Fine/Motor Perceptual.

Table 1. Mean and Standard Deviations for Sensory Processing and factor Summary for Bipolar Group

Sensory Processing	Mean	SD
Section A: Auditory Processing	26.15	5.7
Section B: Visual Processing	34.5	4.2
Section C: Vestibular Processing	43.9*	5.9
Section D: Touch Processing	66.4	12.5
Section E: Multisensory Processing	25.4	4.3
Section F: Oral Sensory Processing	40.9	12.8

Table 1. (Continued)

Modulation		
Section G: Sensory Processing Related to Endurance/Tone	39.09	7.3
Section H: Modulation Related to Body Position	38.6	6.7
Section I: Modulation of Movement Affecting Activity	22.6	3.8
Section J: Modulation of Sensory Input Affecting Emotional Responses	14.1	3.8
Section K: Modulation of Visual Input Affecting Emotional responses	13.9	2.6
Section L: Emotional/Social Responses	49.9*	14.1
Section M: Behavioral Outcomes of Sensory Processing	171*	5.4
Section N: Items Indicating Threshold for Response	11.4	2.1
Factors		
1. Sensory Seeking	53.9*	12.5
2. Emotionally Reactive	42.7*	14.9
3. Low Endurance/Tone	39.0	7.5
4. Oral Sensory Sensitivity	30.0*	11.6
5. Inattention/Distractibility	20.1*	5.5
6. Poor Registration	33.3	5.0
7. Sensory Sensitivity	17.9	6.5
8. Sedentary	14.7	4.0
9. Fine Motor/Perceptual	8.9	3.6

* Indicates Definite Difference Score

DISCUSSION

The present findings offer support for clinical descriptions of children with bipolar disorder. The fact that they obtained Probable or Definite Differences in five of six Sensory Processing areas suggests that these children are highly sensitive to sensory input from the environment. This is similar to Type I Regulatory Disordered children who evidence hypersensitivity to sensory input. The finding that they obtained a Definite Difference in Vestibular Processing is particularly interesting. These children are often described in the clinical literature as “sensation seeking” or “risk taking.” They tend to seek out experiences that excite their central nervous systems. Their method of discharging stimulation is through action and impulse rather than through reflection. Furthermore, when these children are overloaded by stimulus input, we often see them exhibiting a paradoxical response. That is, whereas typical children tend to seek out soothing experiences and welcome comforting by caregivers when their systems are overloaded, children with bipolar patterns often become even more activated, excited and stimulus craving when they are over-stimulated. This is often seen in excited giddiness, rages, or a combination of these behaviors (mixed states) that can be unrelenting.

High vestibular activity may make it very difficult for a child to be available for learning. Seeking exciting stimulation interferes with the ability to engage in reflective thinking. In order for these children to be available to intervention they must first be brought to a calm state. This supports Popper's contention that the bipolar child needs a "haven from rage." Popper (1985) recommended allowing the bipolar child to find a "safe haven" when he/she was upset in order to recover from excitation. The "safe haven" is a place that provides low sensory input and opportunities for self-soothing. For example, occupational therapists have suggested that a tent be set up in an area of the classroom or home so that the child can spend time alone. The enclosed environment may have a soft beanbag chair and stuffed animals to provide soothing stimulation.

Bipolar children obtained Probable Differences in three of six Modulation areas. Modulation refers to the child's ability to down-regulate or to up-regulate behavior in the face of stimulation. Modulation Related to Body Position and Movement refers to the child's ability to move effectively within the environment. For example, we often see these children taking movement or climbing risks during play that compromise their personal safety. Modulation of Movement Affecting Activity Level is a measure of the child's activity level. One of the clinical markers suggestive of a bipolar pattern is the child's high activity level and disinhibited behavior. Modulation of Visual Input Affecting Emotional Response and Activity Level measures the child's use of visual cues to establish contact with others. It may be difficult, at times, to use visual cues when the child has an action orientation.

Findings of Definite Differences in Emotional/Social Response and Behavioral Outcomes of Sensory Processing is highly consistent with behavioral observations of bipolar children. These children have very poor coping strategies. They tend to become dysregulated in situations that most children are able to handle behaviorally. Parents often report that the word "No" has a "special" quality for these children in terms of precipitating a meltdown. Typical children are able to form mental pictures connecting the present situation with the past and the future. These mental representations enable the child to delay and defer gratification. In contrast, children with bipolar patterns have difficulty tolerating frustration and anxiety. They tend to discharge affects in an "action mode" because they have not developed the capacity for symbolizing emotions, specifically anger and disappointment. These emotional experiences result in intense tantrums and frequent rage behavior.

These findings from analyzing individual sensory processing factors are also consistent with our observations of bipolar children. They obtained Definite Differences in the areas that typify reasons for clinical referral, i.e., high sensory seeking, emotional reactivity, and inattention/distractibility. When children are referred for clinical evaluations and exhibit these behaviors and when there is a strong family history of mood disorders, these behaviors should alert clinicians to the possibility that the child may be evidencing a mood disorder.

The present findings are highly consistent with clinical observations of children with bipolar patterns. These findings can be used clinically to add information that can help us make correct diagnoses in children. Children who present the phenom-

enological patterns found in this study are often misdiagnosed and mishandled clinically. For example, a child who is sensory seeking, emotionally reactive, and inattentive/distractible may be diagnosed with Attention Deficit Hyperactivity Disorder and prescribed stimulant medication. Children with bipolar disorder often react adversely to stimulants. The psychopharmacological literature warns about the possibility of mania being triggered by stimulant intervention. Thus, clinicians seeing children who present with patterns described in the present study need to be cautious in terms of diagnosis and treatment. A comprehensive history should always be done to find out if there is a history of mood disorders in the family line.

Limitations

The present study is an initial investigation of sensory functioning in young children who evidence bipolar patterns. There are important weaknesses, however, to consider. First, as a preliminary study, the sample size is small. Replication of the present findings would increase the power of the findings. Second, the present study used a single measure of sensory functioning, and therefore the findings should be viewed cautiously. The Sensory Profile needs to be used in conjunction with other measures of sensory processing to make a definitive diagnosis. Our bipolar sample may be heterogeneous. We need to think about different phenotypes of bipolar patterns. Leibenluft et al. (2003) and Staton (2004) have proposed definitions of different clinical phenotypes of juvenile mania. This is an exciting and fertile research area. We may see that children with different clinical phenotypes have different and very specific patterns of sensory processing and modulation that will enhance and facilitate treatment.

Finally, the present preliminary study compares children with bipolar patterns to the normative sample. It will be important to compare patterns in different diagnostic groups, particularly the ADHD group that has a high degree of overlap with characteristics of bipolar children.

CONCLUSIONS

The DIR[®] Model provides a lens that has not been used in studies of children with bipolar patterns. This lens is developmental in nature and involves looking at how biological factors and environmental factors are translated in parent/child interactions at each functional emotional developmental level. Individual differences in terms of strengths and weaknesses in different areas of sensory processing and modulation abilities will color the child's behavioral presentation, thus resulting in different "patterns." Similarly, each child will present a unique pattern of functional emotional milestones mastered or in need of mastery, further contributing to different behavioral presentations.

At this time, research in childhood bipolar disorder has not been integrated in the fashion that is being suggested. Rather, intensive work is being done in the psychopharmacological arena, pioneering work is taking place in the area of neurophysiology, and attempts are being made to categorize behaviors into different phenotypes, few treatment paradigms with children have been developed thus far. The DIR[®] model is a holistic model that melds each of these areas to give a comprehensive picture of the child's functioning that leads to a tripartite treatment plan involving therapy, home, and school programs.

Finally, the DIR[®] Model enables us to look at bipolar patterns as a severe form of Regulatory Disorder, thus putting it into a familiar context of disorders that involve **both** sensory challenges combined with specific ways in which these challenges are responded to behaviorally. The term "bipolar disorder" in children has been extremely confusing because the behaviors in children are so different from the patterns that we have come to know in adult-onset bipolar. Looking at bipolar disorder within the context of regulatory disturbances provides a clearer picture of the specific components and the specific areas of dysfunction that need to be addressed in each individual child.

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Childhood Onset Bipolar Disorder: Pharmacological Treatment Overview

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Keywords: bipolar, child, diagnosis, pharmacology, treatment

Abstract: *The diagnosis of Bipolar Disorder is still quite controversial in child psychiatry: its boundaries remain uncertain while treatment is based as much on research as on clinical wisdom. Several questions on the treatment of Bipolar Disorder in children await an answer: 1) Does age affect treatments effectiveness and side effects? 2) Can mania be induced by Antidepressant or Stimulant treatment, and if so, how frequent is it? 3) Are there risks associated with long-term exposure to these agents in children? Efficacy data from placebo controlled studies are lacking for most routinely used drugs. Safety and dose-response data are insufficient, and the effects of long term use of these agents in monotherapy as well as in combination therapy await further research. Current knowledge of Mood stabilizing, Antidepressant, Stimulants and Antipsychotic agents in the treatment of Bipolar Disorder in pediatric patients is reviewed, and the potential risks associated with Antidepressants and Stimulants, and general guidelines for the treatment of Bipolar Disorder in children are discussed.*

Introduction

The assessment and treatment of Bipolar Disorder in children is particularly challenging due to extensive symptoms' overlap, sometimes comorbidity, with other psychiatric, medical and neurological disorders (Faedda, Baldessarini, Suppes, et al., 1995).

The latest edition of the Diagnostic and Statistical Manual (DSM-IV-TR, 2000) provides diagnostic criteria for Mania, Depression, Mixed states and Cyclothymia that apply to all ages. In Figure 1 we summarize diagnostic criteria for Bipolar Disorder, Manic. For a comprehensive review of the diagnostic criteria, we refer the reader to the DSM.

Figure 1

Diagnostic Criteria for a Manic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary).
- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
 - 1) Inflated self-esteem or grandiosity
 - 2) Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
 - 3) More talkative than usual or pressure to keep talking
 - 4) Flight of ideas or subjective experience that thoughts are racing
 - 5) Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
 - 6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
 - 7) Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
- C. The symptoms do not meet criteria for a mixed episode.
- D. The mood disturbance
 - 1) is sufficiently severe to cause marked impairment in occupational functioning, usual social activities, or relationships with others,
 - 2) necessitates hospitalization to prevent harm to self or others, or
 - 3) has psychotic features.
- E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

^aAdapted from DSM-IV-TR; manic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, ECT, light therapy) should not count toward a diagnosis of bipolar I disorder.

Bipolar Disorder occurs on a spectrum of different polarities (from mania to depression to normality-euthymia), recurrence rates (chronic, continuously cycling to intermittent or episodic) and severity (from cyclothymia to psychotic forms). Additionally, in the treatment of childhood-onset Bipolar Disorder, developmental factors are often overlooked while the Central Nervous System undergoes dramatic changes through processes of myelination, plasticity and maturation, equally dramatic changes occur in association with language development, emotional regulation, social competency, sexual development and cognitive maturation. These changes affect clinical presentation, treatment response as well as outcome.

Compared to adult forms, pediatric Bipolar Disorder manifests with mixed-dysphoric and labile, rapidly changing presentations. Discrete episodes cannot always be recognized and often a rapid cycling course of Bipolar Disorder is observed in children. Symptoms (and disability) are present more or less chronically, but with fluctuations in the intensity of particular clinical manifestations (Faedda, et al., 1995; Faedda, Baldessarini, Glovinsky, Austin, 2004; Geller, Zimmerman, Williams, Bolhofner, Crane, 2002).

Bipolar Disorder unfolds in different syndromes, various symptoms' patterns, and at different points along the developmental trajectory. In young children, especially boys, chronic mania is common, usually with marked hyperactivity and hostile aggression, while in girls an onset with anxiety disorders or depression is often associated with a Bipolar Disorder type II subtype (Faedda, et al., 2004). In prepubertal children, comorbidity with Learning Disabilities, Sensory integration, Attention Deficit-Hyperactivity, Conduct, Oppositional-defiant or Anxiety disorders further complicates both assessment and treatment. In adolescents, the emergence of eating, anxiety (Panic) or other behavioral disorders or comorbid substance abuse is an added complication and a source of concern.

The high rate of conversion to Bipolar Disorder in childhood Major Depressive Disorder (Geller, et al., 2002) is consistent with the hypotheses that childhood depressive episode can represent the onset of Bipolar-II Disorder in children (Faedda, et al., 1995; Faedda, et al., 2004) as well as in adults (Hantouche, Akiskal, Lancrenon et al., 1998).

Extensive impairment of home, school, social functioning, and sometimes, developmental delays require a multidisciplinary approach to assessment, treatment, and rehabilitation.

In the pediatric population, developmental factors play a role in the child's ability to modulate affect, channel energy, contain aggression or maintain attention. The precocious onset of symptoms can interfere with mastery of effective coping skills and development of problem-solving strategies. This 'behavioral immaturity' in some areas of functioning is in clear contrast with perfectly normal or advanced skills in other areas. Confusion also exists about what is 'normal adolescent behavior' as opposed to psychopathology. Children with Bipolar Disorder may exhibit symptoms intermittently, or as fluctuating patterns. For this reason, sometimes, symptoms are seen as willful or intentional behaviors, and met with stern or punitive attitudes. The difficulty of clearly defining the boundaries of behaviors requiring intervention often delays treatment and maintains dysfunctional behaviors. Symptoms of Bipolar Disorder, including impulsiveness, irritability and moodiness, oppositional-defiant behavior, rigidity and struggles with authority must be distinguished from common, developmentally appropriate testing of limit-setting in teen-agers. However, due to the insidious onset and the sub chronic or chronic course of the illness, parents and teachers might have become habituated to the symptoms of mania, including aggression and disturbances of sleep, activity and concentration or dismiss it as a 'temper' problem. Obtaining very accurate descriptions of the type, duration, frequency and

course of symptoms is the only way of establishing and documenting the pre-treatment baseline, target treatment and monitor outcome.

Pharmacotherapy is often, if not always, the foundation for the successful treatment of Bipolar Disorder in any age group. However, non-compliance with treatment often interferes with a successful outcome.

Pharmacological treatment should always be considered part of a comprehensive therapeutic approach. This requires addressing issues pertaining to lifestyle (sleep hygiene, exercise, diet, socialization) as well as school interventions (addressing learning disabilities and executive functioning deficits), and psychoeducation. The ongoing education of patients and families is crucial in creating a collaborative relationship between health providers and patient. Such collaborative approach encourages reporting and management of side effects, as well as ongoing assessment of treatment response and reinforces compliance with treatment.

Great progress in the knowledge of the clinical features and phenomenology of pediatric onset Bipolar Disorder and, to a lesser degree, of the effective somatic treatments available encourages careful assessment of current clinical practices. As recently summarized in the American Academy of Child and Adolescent Psychiatry (AACAP, 1997) the selection of treatment should be informed by: 1) evidence of efficacy; 2) illness' phase; 3) clinical features; 4) side effect profile of agent; 5) past response to treatment; 6) family and/or patients' preference.

Two main approaches can be recognized in the treatment of Bipolar Disorder in all ages: for the purpose of simplification we'll refer to the two as *symptom-based treatment*, and *stabilization treatment*.

In the *symptom-based treatment*, medications are prescribed to address the most significant symptoms present, including depression (stabilizing from 'below') or mania (stabilizing from above). In this approach Antidepressants are often used, both as acute and maintenance treatment, following the hypothesis that prophylaxis of depression will reduce morbidity and recurrence rate in Bipolar Disorder. Antidepressant treatments are often combined with Mood Stabilizers and/or Atypical Antipsychotic or stimulants during maintenance treatment.

The alternative approach of *stabilization treatment*, which we favor, aims at the treatment and prevention of excitatory states (manic or mixed) as a way of preventing cycling and recurrences. Antidepressants and other Central Nervous System stimulants are avoided, as they carry the potential to induce mania and cycling (see Antidepressant and Bipolar Disorder below). Rather than treating the illness' phases, priority is given to the long-term stabilization of symptoms.

In an effort to summarize the growing body of literature and improve understanding of pharmacotherapy of Bipolar Disorder, we reviewed relevant research and clinical data on Mood Stabilizers, Atypical Antipsychotics, Antidepressants and other agents. This is not a comprehensive review of the vast, and fast growing literature on the subject, but rather an attempt at pointing out some areas of consensus or controversy, as well as topics that require additional research. Most authors provide age range for studies conducted in the pediatric population, mostly on adolescents. However, the data is scarce, and although the relationship between age and response

to specific treatments remains unclear, data on adolescent response are often used to guide treatment decisions in children as well.

Mood Stabilizers

The treatment of Bipolar Disorder in the pediatric population is based on treatments known to be effective in adults. Available data from both, controlled trials and open clinical series support the relative efficacy and safety of Mood Stabilizers used routinely in adults in the acute and maintenance treatment of Mania and Bipolar Disorder type I in adolescents and children.

Several considerations limit the value of the data available, including: 1) small sample size; 2) combination of patients with different bipolar subtypes [type I, II, NOS, Cyclothymia] or distinctive features [euphoric vs. mixed mania, psychotic forms, comorbid diagnoses, inpatient vs. outpatient samples, rapid or ultra-rapid cycling, pre- and post-pubertal cases]; 3) retrospective design; 4) short duration of follow-up; 5) lack of control of comparison group; 6) use of variable diagnostic criteria and outcome measures.

There is a paucity of data on the pediatric use of Mood Stabilizers in monotherapy and in combination, including combination with an Atypical Antipsychotic. Agents used to stabilize mood (MS or Thymoleptics) belong to different categories. Lithium salts, anticonvulsants, some of the Antipsychotics and Neuroleptics have been used in the treatment of manic and mixed states, and in the prevention of recurrences or relapses. Some of the mood stabilizing agents (Lithium and Lamictal, possibly Trileptal) might also have some antidepressant effects.

Lithium

The gold standard pharmacological treatment in adults remains lithium. Discovered in the late '40's by John Cade (Cade, 1949) in Australia and introduced in the United States in the late '60's, lithium is effective as an antimanic agent and in the prophylaxis of manic and depressive recurrences. Data on the efficacy of lithium in the acute treatment of manic or mixed states in the pediatric population is limited (Faedda, et al, 1995). In placebo-controlled studies about 85% of the patients responded to treatment with lithium. In open trials the percentage of response was slightly lower, about 80%. The response to lithium was somewhat higher in cases involving the pure diagnosis of Bipolar Disorder as opposed to cases that involved Bipolar Disorder and comorbid Attention Deficit Hyperactivity Disorder or alcohol abuse (Lena, 1975; McKnew, et al., 1981; DeLong, Nieman, 1983; Geller, et al., 1998).

Open studies and case series show similar rates of response in a mostly outpatient population. Although these are uncontrolled data and positive responses are more likely to be published than negative or inconclusive trials, lithium responsiveness

Table 1. Response to Lithium Treatment in Patients with Pediatric-Onset Mania*†

Blind, placebo-controlled trials‡					
Study	Year	N	Diagnostic Criteria	Improved (%)	Comments
Lena (7)	1979	11	NA	82	Six patients dropped out
McKnew et al. (8)	1981	2	DSM-III	100	Parents lithium-responsive
DeLong et al. (9)	1983	11	NA	100	All relapsed 6 mos. after blind discontinuation
Geller et al. (10)	1998	13	DSM-III-R	60	High rates of Comorbidity (Conduct and substance use)
Total		37		85.5 ± 19[^]	

DSM, APA Diagnostic and Statistical Manual of Mental Disorders, III and III-R editions;

N= number of subjects treated; NA, data not available

*The majority of cases involved adolescents.

† All studies used a cross-over design.

‡ Ages in the controlled studies ranged from 6 to 16 years.

[^]Mean ± SD is weighted mean by n/study; SD=Standard Deviation.

appears to be well established and supported by most clinicians. In open studies and case reports reviewed in 1995 (Faedda, et al., 1995), lithium's antimanic efficacy was 82 % in 186 patients. The dose-response curve of lithium as an antimanic agent in the prepubertal and pubertal pediatric population remains understudied.

The literature on lithium's efficacy in maintenance treatment is also very limited but very consistent in showing benefits measured as sustained remission of symptoms compared to pre-treatment course. Mostly anecdotal reports and case series support the effectiveness of lithium for the prophylaxis of manic and depressive recurrences. Additionally, studying the effect of discontinuing treatment can give us an indication of whether this treatment is really effective. In adults, the effect of discontinuing treatment in patients that have responded to treatment results in high recurrence rates (Faedda, Tondo, Baldessarini, Suppes, Tohen, 1993). The same has been documented in children. Strober et al (Strober, Morrell, Lampert, Burroughs, 1990) reported that after lithium discontinuation 92% of adolescents who had reached stability with treatment experienced a recurrence, compared to a 37% recurrence rate in those that had remained compliant with treatment.

Predictors of a positive response to lithium include a sequence of (hypo)mania-depression-euthymia (Faedda, Baldessarini, Tohen, Strakowski, Waternaux, 1991), lack of Attention Deficit Hyperactivity Disorder symptoms before adolescence (Strober, DeAntonio, et al., 1998), a family history of response to Lithium (DeLong, Aldershof, 1987). A poor response to lithium has been associated with an Axis I diagnosis before age twelve (Strober, Morrell, et al., 1988), the presence of a personality disorder during euthymia (Lena, 1979), a mixed or dysphoric presentation, and a sequence of depression- (hypo) mania-euthymia (Faedda, et al., 1991).

Lithium treatment is delicate, as the therapeutic range is very close to the toxic levels, and close monitoring is recommended. However, under experienced supervision, lithium treatment is safe and usually well tolerated. Before starting treatment with lithium (unless dictated otherwise by medical necessity), it is helpful to obtain: height, weight, vital signs, baseline CBC, LFT's, BUN, creatinine, TSH, T3, T4, electrolytes and a routine urine analysis. Routine monitoring of blood levels and renal and thyroid function, as well as urinalysis are required for the safe long-term or maintenance use of this treatment. Lithium levels should be obtained approximately twelve hours after the last lithium dose.

Most patients treated with lithium salts will experience some side effects. Young patients experience reduced frequency and severity of side effects when compared to adults and the elderly, possibly because their lithium clearance is very efficient. There are, however, exceptions due to individual sensitivity and rates of lithium elimination. The severity of most side effects seems to be reduced by continued use, possibly the result of tolerance. Irritation of the upper gastrointestinal tract is worse if the medication is administered on an empty stomach: for this reason it is recommended that lithium be administered after a meal. In most cases a twice/day (or BID) dosing is used, after breakfast and dinner. The total daily dose is determined either by body weight (Weller, Weller, Fristad, 1986), usually 30 mg/Kg/day in divided doses (in the acute treatment of mania), or following a kinetics-based nomogram (Geller, Fetner, 1989). Neither method is always accurate, (Hagino, Weller, Weller, Fristad, 1998) nor does relying on these methods exempt the clinician from close monitoring of blood levels and side effects. Greater caution should be used when first using this agent, when treating young children, during concurrent medical illnesses and when using the higher mg/Kg doses and associated high serum levels. Blood levels need to be maintained usually between 0.6 and 1.2 mEq/L. Toxicity can manifest in some at levels of 1.4-2.0 mEq/L, but most often levels above 2.5 mEq/L are associated with serious cases of toxicity.

Common complaints, initially even after a meal, include stomach and abdominal cramps, indigestion, heartburn, nausea, vomiting and loose bowel movements or diarrhea. Increased thirst (polydipsia) and frequent urination (polyuria) are also common, and in children this can lead to bedwetting (enuresis); less frequent are weight gain and edema. Tremor, muscle weakness, fatigue or tiredness and ataxia can be frequent complaints. Alteration of taste sensation, hair loss and exacerbation of skin problems, especially acne in adolescents, can further limit the use of lithium in the pediatric population. Reversible abnormalities of cardiac conduction, albeit rarely, have been reported, but their clinical implications are not clear.

Long term effects of lithium on several organs and systems have been reported: the three major ones involve the central nervous system, kidneys and thyroid. The prevalence of these side effects in the pediatric population remains understudied, and their impact on compliance and discontinuation of treatment is unclear.

Lithium effects on Central Nervous System functions can range from fine tremor or impaired coordination to cognitive slowing and memory impairment to toxicity,

with confusion, seizures, and coma. Memory and cognitive difficulties might require treatment discontinuation. Lithium neurotoxicity can occur at blood levels two or more times higher than therapeutic levels.

Prolonged exposure to therapeutic levels of lithium does not alter the renal glomerular function (filtration), but toxic levels of lithium can cause interstitial fibrosis and glomerular sclerosis or tubular atrophy. The tubular function of the kidney, involved in concentrating the urine, is impaired in some adults exposed to lithium. Toxic levels of lithium are often associated with a decreased ability to concentrate urine and, in the most extreme cases to (nephrogenic) diabetes insipidus. In a rare 3-5 year follow-up study of 4 adolescents, renal function remained normal (Khandelwal, Varma, Srinivasa Murthy, 1984).

Lithium has been associated with thyroid enlargement (goiter), hypothyroidism and the development of thyroid autoantibodies (Alessi, Naylor, Ghaziuddin, Zubieta, 1994). Hypothyroidism is sometimes reversible upon discontinuation of lithium.

Anticonvulsants

The use of anticonvulsants to treat children and adolescents with Bipolar Disorder is off-label, as none of the agents is indicated for the treatment of Bipolar Disorder before age 18. Anticonvulsants are often used in pediatric age given the high rate of seizure disorders in this population. There are few studies that have looked at the efficacy of anticonvulsants in children with Bipolar Disorder. Depakote (Sodium Divalproex, Valproic Acid) and Carbamazepine are the agents that have been studied more extensively.

Sodium Divalproex and Valproic Acid

Sodium Divalproex (Depakote) and its metabolite, Valproic Acid have been found to be effective in adolescents with acute mania in over 60 % of the cases (Papatheodorou, Kutcher, Katic, Szalai, 1995; Kowatch, Suppes, Carmody, et al., 2000; Wagner, et al., 2002; Chang, et al., 2003).

Table 2. Response rate to Anticonvulsants in Patients with Pediatric-Onset Mania

Response to:	N	%
Valproate		
Papatheodorou et al	15	60.0
Kowatch et al	11	46.0
Wagner et al	40	62.0
Chang et al	23	78.0
Donovan et al	20	80.0
Henry et al	15	53.3

Table 2. (Continued)

Carbamazepine		
Bouvard et al	11	63.3
Kowatch et al	10	34.0
Lamotrigine		N/A
Gabapentine		N/A
Findling et al		
Lithium + Valproate	90	46.6
DelBello et al		
Topiramate add-on	26	73.1
Kowatch et al	20	80.0
Combined treatment		

In a recent comparison of lithium, Valproic Acid and Carbamazepine, Kowatch (Kowatch, et al., 2000) reported a response rate (Clinical Global Impression: much improved or improved) of 46, 40 and 31 percent, respectively, and even lower rates of response as measured by a 50% decrease in the Young Mania Rating Scale score. In a double-blind, placebo-controlled crossover study, Donovan et al. (Donovan, et al., 2000) reported an 80% response rate after 6 weeks of treatment with mean blood levels of 82 mg/ml.

A retrospective review of response to Valproic Acid in 15 patients (4-18 year old) with Bipolar Disorder by Henry et al. (Henry, Zamvil, Lam, Rosenquist, Ghaemi, 2003) confirmed the efficacy of Valproic Acid in 53%, although weight gain was reported in 27%. Deltito et al. (Deltito, Levitan, Damore, Hajal, Zambenedetti, 1998), in an open study of Valproic Acid among adolescent inpatients in Sweden, observed improvement of symptoms of mania, psychosis, agitation and aggression. Davanzo (Davanzo, et al., 2003) compared the efficacy of lithium, Valproic Acid and Carbamazepine. In this retrospective study of treatment response in inpatient pre-adolescents, Clinical Global Improvement ratings were significantly better after two weeks of treatment among patients receiving lithium or Valproic Acid than in those treated with Carbamazepine.

Frequent side effects reported with Depakote include sedation, gastrointestinal upset, nausea, vomiting and loose bowel movements. Increased appetite and weight gain have also been reported, and can reduce compliance or lead to discontinuation of treatment. Alopecia, decreased serum carnitine levels, hyperglycemia and menstrual irregularity have been described. Rare hepatic toxicity and acute hepatic failure have been reported in very young children, mostly below two years of age, treated with Valproic Acid in combination with other anticonvulsants. Increased levels of ammonia sometimes leading to Central Nervous System toxicity and coma, pancreatitis and blood dyscrasias, including aplastic anemia, have been reported as well.

In adolescents elevated levels of testosterone have been reported, and in women this has been associated with polycystic changes of the ovaries, menstrual irregularities including amenorrhea, and increased insulin resistance (Isojarvi, Laatikainen, Pakarinen, Juntunen, Myllyla, 1993; Isojarvi, Laatikainen, Knip, et al., 1996; Isojarvi, et al., 1998). These changes are usually reversible, but since most data derive from the use of this medication among children suffering with seizure disorders, the generalization of these findings to the general population might not be appropriate.

Blood levels between 50-120 mcg/mL are commonly used although a dose-response curve for mania in children and adolescents has not been obtained.

Carbamazepine

Carbamazepine, a tricyclic anticonvulsant (dibenzazepine) is effective in the treatment of adults with mania, and may be effective in pediatric Bipolar Disorder, alone or combined with lithium. Carbamazepine has been used to treat a host of affective, behavioral, and neuropsychiatric disorders in children and adolescents, including Attention Deficit Hyperactivity Disorder, conduct disorder or aggression. However, not all studies have confirmed the efficacy of carbamazepine in these syndromes. Cueva et al. (Cueva, et al., 1996) in a double blind, controlled study in 22 children (5-12 years old) diagnosed with conduct disorder and hospitalized for aggression did not find a statistically significant difference between placebo and carbamazepine.

Several case reports, however, support the effectiveness of carbamazepine in the treatment of aggression and attention deficit hyperactivity disorder-like behavioral disorders in children. Bouvard et al (Bouvard, Bayle, Dugas, 1993), showed a positive response in about 80% of children with Bipolar Disorder. In adults and in children carbamazepine seems to be most helpful in cases of mixed states and dysphoric mania. Blood levels for optimal maintenance treatment usually fall within the anti-epileptic therapeutic range. This is measured 12 hr after the last dose and is preferably maintained within a range of 6-12 mcg/mL.

Side-effects in 220 patients under age 16 with seizure disorders treated with carbamazepine were similar to those found in adults (Pellock, 1987). They included excessive sedation (43%), vertigo or ataxia (26%), mild cerebral intoxication (tremor, slurred speech, diplopia, movement disorder) or headache (16%); nausea and vomiting or other gastrointestinal complaints (9%), and rashes or other dermatological reactions (5%). Rare but serious reactions to carbamazepine include blood dyscrasias (most often leucopenia, ca. 2% risk), or, much less often anemia or platelet deficiencies; these reactions, although typically mild do not differ in frequency or severity between children and adults. However, for this reason regular blood count monitoring is required (Tohen, Castillo, Baldessarini, Zarate, Kando, 1995).

Carbamazepine can induce spina bifida or facial malformations in the fetus if taken during pregnancy (Kaneka, Kondo, 1995). Carbamazepine is also a powerful

inducer of microsomal oxidases in the liver. As these enzymes are used in the metabolism of several drugs (including carbamazepine), this can lead to significant decreases in blood concentrations of carbamazepine and other agents, sometimes complicating treatment with multiple agents.

Although carbamazepine does not exert any pharmacological action like those of structurally analogous antidepressants, it may induce mania or excitement in some children (Faedda, et al., 1995).

Trileptal

Trileptal, or oxcarbazepine, is an analog of carbamazepine. Unlike carbamazepine, rather than undergoing metabolic oxidation to a 10, 11 epoxy- metabolite that induces the liver enzymes, Trileptal converts into a 10-monohydroxide derivative. Many interactions found when carbamazepine is used in combination with other drugs are not an issue with Trileptal. Even the side effect profile is quite different and very benign for Trileptal, unknown to cause the more serious side effects like aplastic anemia or hepatotoxicity. Mild side effects like sleepiness, headache, dizziness, double vision, unsteady gait, vomiting, rash, and abdominal pain have been associated with Trileptal treatment.

No controlled data exists on the use of Trileptal in children with Bipolar Disorder. However, open data (Emrich, Altmann, Dose, von Zerssen, 1983) and controlled trials also indicate that oxcarbazepine has antimanic effects in bipolar adults (Dietrich, Kropp, Emrich, 2001). The broad spectrum of action, a benign side effect profile, the reported safety in children and ease of use (especially the lack of interaction with other drugs and the fact that blood levels are not routinely required for proper monitoring), have contributed to the widespread use of this agent as a Mood Stabilizer. Trileptal alone or in combination with other Mood Stabilizers or Antipsychotics has become, in spite of the lack of controlled studies, a first line agent in the treatment of pediatric Bipolar Disorder.

Other Anticonvulsants

No controlled studies of Lamotrigine or Gabapentine have been conducted, and the only data supporting their use comes from case reports.

Lamotrigine has been used successfully in the stabilization of adults with Bipolar Disorder. Its efficacy in ameliorating symptoms of depression and some mixed/rapid cycling states has been an extraordinary addition to the available treatments for Bipolar Disorder.

Concerns about its potential for inducing rashes, sometimes progressing to the feared Stevens-Johnson syndrome remain, but a slower, more careful titration schedule has drastically reduced the likelihood of these reactions.

Lamotrigine has no antimanic properties in adults, and it might actually cause dose-dependent behavioral disinhibition and hypomania. Common (>5%) side effects include dizziness, unsteady gait, somnolence, headache, double or blurred vision, nausea, vomiting, and rash. Dizziness, diplopia, ataxia, blurred vision, nausea, and vomiting are usually dose related. Lamotrigine does not appear to cause weight gain, and it interferes with other commonly used Mood Stabilizing treatments, especially anticonvulsants. For instance, the addition of Valproic Acid increases lamotrigine steady-state concentrations in normal volunteers by slightly more than 2-fold.

Gabapentine (Neurontin) is used as an add-on Mood Stabilizing agents in adults with Bipolar Disorder, although it is not an effective antimanic in monotherapy. Significant behavioral disinhibition in children with seizure disorders has been reported, and caution with this agent should be used until safety and efficacy data becomes available.

Combined treatment

The use of various combinations of Mood Stabilizing agents is supported by open data and clinical experience. Lithium being the gold standard of pharmacologic treatment of manic depressive illness, most research has been focused on the benefits of adding an anticonvulsant to lithium.

In a series of nineteen treatment-resistant adolescents with Bipolar Disorder, Garfinkel et al. (Garfinkel, et al., 1985) found lithium and carbamazepine in combination to be more effective than monotherapy during manic and mixed states. In a 6-month, prospective study of the efficacy of a combination of two Mood Stabilizers in patients with Bipolar Disorder (mean age 11 years) who had failed to respond to a single Mood Stabilizer, Kowatch et al. (Kowatch, Sethuraman, Hume, Kromelis, Weinberg, 2003) reported an 80% response rate.

In one study using a combination of lithium and Valproic Acid, Findling (Findling, et al., 2003) found that less than 50% of the cases responded. In another add-on study by DelBello et al, (DelBello, Kowatch, et al., 2002) Topiramate produced a very high response rate of 73% when added on to Valproic Acid. In most cases, treatment with a Mood Stabilizers is combined with an Antipsychotic until the patient is stabilized, and then an attempt at removing the Antipsychotic (or the Mood Stabilizer) is made, so that the treatment regimen can be simplified, and associated side effects can be reduced. Caution has to be used as to not cause a recurrence of Bipolar Disorder by early or abrupt changes to an effective regimen. If a comorbid condition (anxiety disorder, Attention Deficit Hyperactivity Disorder) requires treatment with an Antidepressant, this should be preceded by stabilization of the mood disorder.

Antipsychotic drugs

Antipsychotic agents are commonly used in the treatment of Bipolar Disorder because of their antimanic effects and sedating properties but also due to the relatively slow onset of therapeutic action with most Mood Stabilizers. Furthermore, an antipsychotic agent might be specifically indicated given the high rate of psychotic symptoms in pediatric Bipolar Disorder (Faedda, et al., 1995). However, there is evidence that treatment with Mood Stabilizers alone can produce (given enough time) a full remission of psychotic symptoms (Varanka, Weller, Weller, Fristad, 1988; Horowitz, 1977).

In an attempt to quantify the prevalence of use of antipsychotics among pediatric patients, Bhangoo et al. (Bhangoo, et al., 2003) reported that 77% of 86 children had had a trial of an antipsychotic, mostly risperidone (58%), olanzapine (35%), and quetiapine (26%) and 12% reporting a trial of a typical neuroleptic; an additional 4% had been treated with ziprasidone, and 1% with clozapine. Overall, 38% of the children had had a trial of an antipsychotic without having had a trial of lithium.

A distinction is made among antipsychotic agents: traditional, also called neuroleptics, and atypical antipsychotics. Traditional antipsychotics are rarely used, owing to their propensity to induce extra pyramidal side-effects (Parkinsonism) but also Tardive Dyskinesia. As Antipsychotics have almost completely replaced neuroleptic drugs, we will discuss primarily these agents. The mechanism by which this group of compounds exerts its effects is not well understood. Atypical Antipsychotics like neuroleptics, block dopamine D2 receptors; their blockade might be more readily reversible, accounting for a reduced incidence of extra-pyramidal side-effects and Tardive Dyskinesia, higher tolerability and greater compliance. In all these compounds, the primary function of dopaminergic and serotonergic antagonists is associated with, and perhaps modulated by, stimulation and/or inhibition of the activity of other receptors including alpha-adrenergic, cholinergic-muscarinic, and histaminergic.

Elevated prolactin plasma concentration with all antipsychotics is secondary to their dopamine D2 receptor antagonism. Hyperprolactinemia causes galactorrhea, amenorrhea, gynecomastia, impotence or decreased libido and can predispose to osteoporosis and cardiovascular disease. All patients should be monitored for the development of these complications (Stoll, et al., 1999).

Atypical Antipsychotics are grouped based on their chemical structure: the dibenzepines (clozapine, olanzapine, and quetiapine) and the benzisoxazoles (risperidone and ziprasidone). Significant differences exist between agents in the same group, but compared to the traditional antipsychotics (e.g. phenothiazines) the Atypical Antipsychotics usually have increased affinity for serotonergic (5-HT₂) receptors over dopaminergic (D₂) receptors. In addition, as a result of their greater affinity for the limbic system than for the basal ganglia, antipsychotic agents cause significantly less extrapyramidal side effects.

Clozapine

In a case series of five children and adolescents with mixed mania, non-responsive to neuroleptic, Kowatch et al. (Kowatch, Suppes, Gilfillan, et al, 1995) reported successful treatment with clozapine (Clozaril). Clozapine has been used successfully in long term prophylaxis of treatment-refractory prepubertal children as well as adolescents with Bipolar Disorder (Faedda, unpublished data, 2004). The use of this agent is limited by the requirement of weekly monitoring of WBC, to reduce the risk of potentially fatal agranulocytosis. Other common side effects include weight gain, excessive salivation, sedation, lowering of seizure threshold and myocarditis.

Risperidone

Buitelaar et al (Buitelaar, van der Gaag, Cohen-Kettenis, Melman, 2001) conducted a 6-week double-blind, randomized, parallel-group design trial of risperidone in the treatment of aggression in hospitalized adolescents with a primary diagnosis of DSM-IV disruptive behavior disorders and with subaverage intelligence. Risperidone-treated patients (N=19) received an average dose of 3mg/d. A statistically significant improvement in the outcome measure (CGI-Severity of illness score) was reported along with the rapid deterioration in all outcome measures during a wash-out discontinuation phase. In a retrospective chart review by Frazier et al. (Frazier, et al., 1999), risperidone (Risperdal) was effective in 80% of 28 children suffering with Bipolar Disorder manic or mixed, with a significant reduction of manic and aggressive symptoms. About 70% obtained some relief from their psychotic symptoms, while only 8% experienced an improvement in Attention Deficit Hyperactivity Disorder symptoms. Risperidone can prolong the QT interval, producing a risk for arrhythmias or sudden cardiac death and should not be used in patients with underlying QT prolongation or concurrently with other agents known to prolong the QT interval.

Quetiapine

After an initial case report of the efficacy of quetiapine (Seroquel) in childhood mania by Schaller and Behar (47), DelBello et al. (DelBello, Schwiers, Rosenberg, Strakowski, 2002) reported almost an additional 50% response when quetiapine (Seroquel), was added to Depakote in inpatient children and adolescents with Bipolar Disorder. The induction of cataracts in beagle dogs treated with high doses for 6-12 months has prompted further clarification of the causes of this potentially troublesome side effect investigating the outcome after 1-year follow-up in monkeys. A striated appearance of the anterior lens surface was detected in 2/7 females at a dose of 225 mg/kg (5.5 times higher than the recommended human dose calculated in mg/m² basis). Reports of lens changes in humans has not been clearly been attrib-

uted to quetiapine treatment. An ophthalmic slit-lamp examination, prior to and every 6 months during treatment, is recommended.

Elevated liver function tests were reported in up to 6% of patients treated with quetiapine, compared to 1% with the other Antipsychotic agents. This effect is usually detected and resolves spontaneously within the first month of treatment even when treatment is continued.

Olanzapine

Olanzapine (Zyprexa), approved by the FDA for acute treatment of mania in adults, was studied by Soutullo et al. (Soutullo, Sorter, Foster, McElroy, Keck, 1999) in a series of seven adolescents meeting DSM-IV criteria for mania, and found to be markedly to moderately effective in 5/7 patients (71%). More recently olanzapine was found to be rapidly effective in 3 prepubertal cases (Chang, Ketter, 2000). Unfortunately reports of high rates of discontinuation due to side effects (especially weight gain and sedation) have reduced its appeal. Its use in child psychiatry as anti-manic and as a mood stabilizer (Krishnamoorthy, King, 1993; Selva, Scott, 2001) has rapidly increased, in spite of concerns of weight gain or sedation (Alfaro, et al., 2002), an increased risk of hyperinsulinemia and the development or worsening of type II diabetes mellitus (Bhangoo, et al., 2003).

Elevated prolactin plasma concentration with all antipsychotics is secondary to their dopamine D2 receptor antagonism. Hyperprolactinemia causes galactorrhea, amenorrhea, gynecomastia, impotence or decreased libido and can predispose to osteoporosis and cardiovascular disease. All patients should be monitored for the development of these complications (Stoll, et al., 1999).

Aripiprazole

Aripiprazole (Abilify) is the first and only dopamine D2 partial *agonist* (with functional 5-HT2A antagonist, and 5-HT1A partial agonist profile). Other Antipsychotic agents, like clozapine, but not typical antipsychotic drugs (e.g. haloperidol), produce significant increases in dopamine and acetylcholine release in the medial prefrontal cortex in rats. It has been hypothesized that this might be the basis for its ability to improve cognitive function.

Aripiprazole can cause insomnia and for this reason is usually given in the morning, in doses from 2.5 to 30 mg daily. The most common side effects reported in adults include headache (32%), anxiety (25%) and insomnia (24%), nausea (14%) and vomiting (12%), dizziness (11%), constipation (10%) and akathisia (10%). Sleepiness is usually reported with higher doses.

Miscellaneous

Other agents are sometimes used in the treatment of children with Bipolar Disorder, including antihistamines (Benadryl) used as a mild sedative and safe sleep aid; Antihypertensive agents like Clonidine, are used for its sedating properties but a powerful depressant of the Central Nervous System; Benzodiazepines, especially lorazepam and clonazepam are used as sedatives, although on occasion they can produce disinhibition in children, and carry a potential for addiction, abuse and contraband among adolescents. Other benzodiazepines, typical antipsychotic like Thorazine and different sleep aids including Zolpidem, Zaleplon or Melatonin, are used both in mania, depression and mixed states. Calcium-channel blockers have been studied after some anecdotal reports, but remain as an option in cases where more traditional treatments fail.

Omega 3 free-fatty acids have been found effective as an add-on in adults with Bipolar Disorder by Stoll et al. (Stoll, et al., 1999); they seem to help mostly depression and mood lability and there is a placebo-control study in adults that shows their efficacy. There are no studies in children but anecdotal reports and our personal experience suggests a possible role in some forms of mood instability.

Antidepressants

Antidepressant agents have been grouped according to their structure (Tricyclic and tetracyclic, TCA), their mechanism of action (serotonin-reuptake inhibitors, SRI), or neither (venlafaxine, bupropion, nefazodone).

These agents differ in pharmacologic action and potency, but also in side effect profile and half-life. As SSRI are the most common type of Antidepressants currently used, we will focus primarily on these agents. Among the SSRI, relative potency (ability to block the re-uptake of serotonin at the synaptic level) was citalopram > paroxetine > fluvoxamine > sertraline > clomipramine > fluoxetine. Potency is not related to efficacy, as all these compounds are effective Antidepressants.

Antidepressants differ in their half-life, presence of active metabolites, effects on the hepatic cytochrome P450 isoenzymes (and therefore on all drugs metabolized by this system). Side effects commonly encountered with SSRI include nausea, diarrhea, changes in appetite and weight, headaches and migraines in those predisposed, but also tremor, jitteriness, excessive sweating, vivid dreams and sexual dysfunctions (anorgasmia, delayed ejaculation). The SSRI antidepressant offer many advantages compared to TCA and MAOI, including safety in overdose, ease of administration (once daily vs. 3 times daily) and a milder side effect profile. A routine medical evaluation (but no blood work) is usually recommended prior to initiating treatment with an Antidepressant. Antidepressants usually require several weeks before a full response is obtained, and treatment is usually continued for several months, as prophylaxis against relapse or recurrence of depression. This practice, however, is not

based on scientific evidence in children with Bipolar Disorder, as discussed in the next section.

Antidepressants use is often suggested by the presence of depressive symptoms during phases of bipolar depression or mixed states, or for the treatment of comorbid anxiety disorders or Attention Deficit Hyperactivity Disorder.

The efficacy of Antidepressants in pediatric patients with Major Depression has been established for Fluoxetine, Paroxetine and Sertraline. Other agents are indicated for the treatment of Obsessive Compulsive Disorder or Social Phobia, but are commonly prescribed for treatment of depression.

Symptoms of depression, anxiety or school problems often prompt an evaluation and can lead to one or more trials of Antidepressants. Depression, with its devastating effects on home and school functioning, is more readily identified. Families are willing to accept the diagnosis and pharmacological treatment is usually recommended and accepted.

Antidepressants and Bipolar Disorder

Concerns about the effects of exposure to Antidepressants in Bipolar Disorder stems from fairly substantial evidence in adults that:

- mania may be induced or worsened,
- cycling is induced or accelerated, and
- response to mood stabilizers is diminished or impaired.

Most pediatric forms of Bipolar Disorder are latent and might manifest fully only when exposed to a life stressor, sleep deprivation, trauma or the pharmacological induction of mania, or 'switch' (Faedda, Glovinsky, Austin, Baldessarini, 2004). All Antidepressants are capable of inducing (hypo)mania, although tricyclic Antidepressants might be the most likely to cause a switch.

Using current diagnostic criteria, rates of Bipolar Disorder in adolescents are around 1%, similar to the rate of mania or BP-I in adults. If duration criteria for episodes of mania and depression are dropped, the rate of sub-syndromal Bipolar Disorder raises to 6.7% (Lewinsohn, Klein, Seeley, 1995). Yet, many forms of early-onset depression (Geller, et al., 2002) and dysthymia (Kovacs, Akiskal, Gatsonis, Parrone, 1994) can evolve or convert to a form of Bipolar Disorder. Some predictors of conversion are known, but the prevalence of the different Bipolar Disorder subtypes in the pediatric population remains unclear.

An onset with dysthymia, depression or mixed states, rather than mania (1-3) is common in Bipolar Disorder. Strober et al. (Strober, Carlson, 1982) and Akiskal et al. (Akiskal, Downs, et al., 1985) described features predictive of a bipolar outcome. Obviously this is quite important, as many forms of Bipolar Disorder manifest with one or several episodes of depression, and only later on start exhibiting (hypo)manic symptoms. The potential effect of some treatments on the course of Bipolar Disorder must be taken into account. In these children depression can onset very early and the

onset of the depression can be sudden and dramatic (most of the time precipitated by a life-event), or subtle and insidious with gradual deterioration of functioning (2). When we treat children with depression we might actually be treating children with an early onset of Bipolar Disorder that has remained latent.

Common predictors of a conversion to Bipolar Disorder include significant psycho-motor retardation, psychotic features, a family history of Bipolar Disorder and a history of antidepressant induced (hypo)mania. Activation with Antidepressants, which is sometimes considered a trivial side effect of these medications, should rather be seen as a risk factor for the development or the precipitation of Bipolar Disorder. According to DSM, (hypo)mania induced by antidepressants is considered an organic mood disorder, distinguished from Bipolar Disorder. Nevertheless, symptom profile and longitudinal course of patients experiencing an episode of Antidepressant-induced (hypo)mania support the hypothesis that these are forms of Bipolar Disorder.

Akiskal (Akiskal, et al., 1985) showed that the specificity of pharmacologically induced (hypo)mania (with decreased sleep, increased activity and increased risk-taking behaviors) in predicting a bipolar outcome was 100%, and the others predictors listed before had a somewhat lower specificity. We found frequent adverse reactions in the treatment history of children with Bipolar Disorder, and believe that they are the most vulnerable subgroup.

In a large prospective study of the psychobiology of depression (Akiskal, Maser, et al., 1995), 955 patients with Major Depression were evaluated at onset and at intervals for up to 10 years. The majority (N= 559) did not manifest any symptoms of mania or hypomania at the first evaluation, but after ten years of follow up, about 70, or 12.5 % ended up converting to a bipolar diagnosis which alerts us to the fact that again, depression can be the first, and often the only, manifestation of Bipolar Disorder for quite some time before manic and hypomanic symptoms are recognized.

The predictors of bipolar outcome in adults with major depression were four basic features derived from questionnaires completed at the initial evaluation. Mood lability, increased energy/activity, daydreaming (in children it should be considered a form of racing thoughts), and social anxiety. Geller and colleagues (Geller, Zimmerman, Williams, Bolhofner, Craney, 2001) completed a 10 year follow-up of 72 children (mean age 10 years). These children had a diagnosis of major depression and excluded specifically children with Bipolar Disorder, Attention Deficit Disorders and children with psychosis. It excluded most of those cases that we know are at high risk for converting into bipolar. After ten years of follow up, 48% of these children had converted to Bipolar Disorder. One third had converted into Bipolar I and a smaller number converted to Bipolar II. Suicidality was frequent at 20%, which is the rate of suicidality found in adults with untreated Bipolar Disorder.

The prevalence of induction of manic symptoms with antidepressants and other treatments like stimulants remains unclear. The occurrence of a manic switch in children with depression that have been treated with antidepressants is still controversial. Geller et al. (Geller, Fox, Clark, 1994) found almost a 32% rate of conversion or

manic switch in children with depression treated with antidepressants. In a review of published reports of approximately 250 cases (Faedda, et al., 1995) the rate of manic switch was 25%, while Rao (Rao, et al., 1995) estimated a conversion rate to Bipolar Disorder of 20% in adolescents initially diagnosed with unipolar depression.

Recently renewed interest in the efficacy, safety and side effect profile of Antidepressants was due to reports of aggressive or violent and suicidal behaviors in children exposed to these drugs. The widespread use of these agents is also a concern, as close supervision by a specialist is often replaced by infrequent visits to the pediatrician.

While several types of adverse reactions can occur with Antidepressants, their severity varies and diagnostic implications are not clear (Faedda, et al., 2004; Strober, Carlson, 1982; Akiskal, et al., 1985). Adverse responses to Antidepressants resemble manic syndromes, and vary in severity and duration, sometimes only reaching hypomanic severity, and remitting with the discontinuation of the inducing agent, and other times reaching psychotic features or extreme cycling, or following a chronic course.

The more troublesome Antidepressant side effects for a patient with Bipolar Disorder are decreased sleep, agitation, impulsivity, akathisia, suicidal behavior and psychosis. Suicidal and violent behavior has been recently the focus of intense scrutiny by American and European regulatory agencies. However, the safe use of this medication in most patients suggests that a subgroup might be particularly 'vulnerable' to Antidepressant treatment. Indeed, the most vulnerable to these adverse reactions to AD treatment might well turn out to be a 'latent bipolar'.

Children who progress to manifest Bipolar Disorder often present with depressive-dysthymic, anxiety, or attention-deficit symptoms long before 'classic' manic symptoms appear, and clarify the diagnosis (Faedda, et al., 1995; Faedda, et al., 2004; Geller, et al., 2003; Strober, et al., 1998; Kovacs, et al., 1994). More often Bipolar Disorder presents as dysphoric irritability, moodiness, explosive outbursts, aggression and oppositional-defiant behaviors. These symptoms are often mistaken for depression, and encourage trials of antidepressant or stimulant treatment.

Exposure of children and adolescents to mood-elevating agents is common in the US. In 900,000 subjects "the 1996 prevalence of any psychotropic medication among youths younger than 20 years was remarkably similar (5.9%-6.3%) across all 3 sites, with stimulants and antidepressants consistently ranked first and second" (Zito, et al., 2003).

Subjects at risk for Bipolar Disorder are prone to develop psycho-motor agitation, anxiety, aggressive, suicidal or homicidal behavior, associated with cardinal symptoms of manic excitement like decreased sleep, physical tension or restlessness, racing thoughts, intense mood swings or persistent and severe irritability.

In a study of treatment-emergent mania, we recently looked at exposure to Antidepressants among subjects with a current diagnosis of Bipolar Disorder by DSM-IV criteria and the prevalence of Treatment-emergent mania as defined by strict operational criteria (Faedda, et al., 2004).

Of 82 patients with Bipolar Disorder, 84% had been exposed to at least one trial of a psychotropic drug and 70% received a mood-elevating agent. Only 29% had no known exposure to a mood-elevating agent and 16% had received no psychotropic medicine.

Among 57 patients treated with Antidepressants and/or stimulents 28% had been given at least an antidepressant but no stimulant, 18% had been given a stimulant but no antidepressants, and 23% were exposed to both. Several of the 82 patients were exposed to multiple agents, including Mood Stabilizers, Antipsychotics, and others.

Operationally-defined (Faedda, et al., 2004) treatment-emergent mania was diagnosed in 33 (58% of 57 cases exposed): 33 of these events was associated with use of an antidepressant (75.7%), or a stimulant (24.2%). One case was associated with carbamazepine treatment, while a corticosteroid was implicated in the other case. None of the treatment-emergent mania was associated with Mood Stabilizers, Antipsychotics, or other psychotropic agents. Among the 33 instances of treatment-emergent mania, ten involved new manic or mixed syndromes, and 23 were acute exacerbations of a previously diagnosable Bipolar Disorder. Bipolar Disorder was first diagnosed following treatment-emergent mania in 14 children. Initial symptoms of emerging mania included marked mood change (100% of cases; especially irritability or anger), sleep disturbances (86%), increased activity (restlessness, agitation; 91%), impulsive or aggressive behavior (77%) with self-injury (20%), suicidal ideation (14%) and suicidal acts (6%). Hypersexual behaviors and pressure-of-speech also were commonly reported.

These symptoms resolved rapidly (typically within two weeks) when the AD/S was discontinued, supporting the conclusion that these outcomes were treatment-related. The Antidepressant was stopped in 94 % of cases and reduced in the rest. Sedating, antimanic treatment with Mood Stabilizing or Antipsychotic agents was recommended in 83% of cases. New onset of psychosis (12%) or homicidal ideation (6%) contributed to hospitalization of 4 patients (12%); in 3 other cases hospitalization was refused, suggesting that inpatient treatment may be needed in at least 20% (7/33) of children with Bipolar Disorder experiencing treatment-emergent mania.

Antidepressants were much more likely to be involved in the precipitation of mania than stimulants. Treatment-emergent mania occurred in 44% of those exposed to Antidepressants and in less than 18 percent with stimulants. Female gender was a risk factor as there were twice as many girls as boys experiencing Treatment Emergent Mania. The exposure to a mood elevating agent obviously was a risk factor and the early onset of anxiety symptoms seemed to predict the onset of (hypo)mania after treatment with a mood elevating agents (Faedda, et al, 2004).

Given the lack of data indicating the short and long term safety of AD/S in patients with Bipolar Disorder, great caution should be used. The use of Antidepressants in adults with Bipolar Disorder is often associated with a Mood Stabilizer as a measure to prevent or mitigate the effects of the Antidepressant, and reserved for necessary situations. Many colleagues involved in the long term treatment of Bipolar Disorder use Antidepressants very sparingly, in sharp contrast with current practices in both adult and child psychopharmacology.

Misdiagnosis of Bipolar Disorder and the difficulties in differentiating Bipolar Disorder from other conditions is a risk factor for exposure to drugs that are not only ineffective but actually dangerous. If an antidepressant is prescribed, treatment should be started with low doses, closely monitored and used in combination with a Mood Stabilizer. As soon as an antidepressant effect is obtained, an attempt should be made at tapering the Antidepressant to assess the need for continued treatment and to decrease exposure to these, potentially destabilizing, treatments.

Stimulants

Often used for the treatment of Attention Deficit Hyperactivity Disorder and sometimes for the treatment of depression, stimulants are extensively used among the pediatric population. Given high rates of comorbidity and misdiagnosis, many juveniles with Bipolar Disorder are exposed to mood-elevating agents (Faedda, et al., 1995; Faedda, et al., 2004), Faedda, et al., 2004; Wozniak, et al., 1995), or abuse them (Woodworth, 2000). The American Academy of Child and Adolescent Psychiatry (AACAP, 1997) recommended that: "Psychostimulants must be used with caution in patients with Bipolar Disorder and are best avoided during acute manic phases." More recently, the AACAP Practice Parameters for the use of Stimulants (Greenhill, Pliszka, Dulcan, 2001) asserted that "Stimulants do not precipitate young adult Bipolar Disorders in boys comorbid for both Attention Deficit Hyperactivity Disorder and non-psychotic Bipolar Disorder on mood stabilizers, either acutely or later on (Carlson, Loney, Salisbury, Kramer, Arthur, 2000)." These statements imply that stimulant treatment in children with BPD is relatively safe, but this point of view is controversial and needs to be reconsidered in light of emerging new research data (Faedda, et al., 2004).

In adults with Bipolar Disorder, stimulant-abuse increases affective and behavioral instability and limits response to treatment with Mood Stabilizers (Baldessarini, Tarazi, 2001). The potential for specific adverse psychiatric responses among patients with known or latent Bipolar Disorder, particularly during treatment with stimulants or other mood-elevating agents unopposed by Mood Stabilizers has been reported (Faedda, et al., 1995; Koehler-Troy, Strober, Malenbaum, 1986). Moreover, adverse psychiatric consequences may include a worse course of Bipolar Disorder long after stimulant treatment in youth (DelBello, Soutullo, et al., 2001; Mota-Castillo, et al., 2001; Soutullo, et al., 2002). A recent issue of the *Journal of Child and Adolescent Psychopharmacology* (2003; 13:2) devoted to the issue of switching has not addressed the implications (diagnostic, therapeutic and prognostic) of treatment-emergent mania, or clarified their prevalence.

Conclusions

Bipolar Disorder causes significant morbidity and mortality, and the manifestation of the illness are quite varied and pleiomorphic. Misdiagnosis is an obstacle to early and effective treatment that can help offset the consequences of Bipolar Disorder on academic, social and interpersonal as well as individual psychological functioning. Treatment with Mood Stabilizers and Atypical Antipsychotics is usually effective, although perhaps higher rates of polypharmacy are necessary in the pediatric population compared to adults.

We suggest that the following guidelines might be of assistance:

1. Sleep hygiene, a caffeine-free diet, regular physical exercise, and discontinuation of stimulants, antidepressants or other agents (steroids, cocaine) that can cause (hypo)mania will help assess the patients' symptoms and the need for further pharmacological treatment;
2. Acute treatment of mania and stabilization with Mood Stabilizers and/or Antipsychotic agents must be attempted before comorbid diagnoses like Attention Deficit Hyperactivity Disorder or Obsessive Compulsive Disorder are treated;
3. An assessment of comorbid diagnoses should be repeated following a period of mood stabilization, as symptoms of Attention Deficit Hyperactivity, Oppositional Defiant, Obsessive-Compulsive and Anxiety Disorders might improve or resolve with the remission of Bipolar Disorder.
4. Treatment of comorbid sleep disorders or residual sleep disturbances can contribute to the patient's stabilization;
5. The use of antidepressants and/or stimulants should be limited in dose and duration, and closely monitored pending short and long-term safety data for their use in children with Bipolar Disorder;
6. Close monitoring of compliance, blood levels, side effects and growth can result in maximum benefits;
7. Interventions to reduce the stressful effects of school and home life and improve patients' and families understanding of treatment are extremely valuable.

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The Use of Developmental, Individual Difference, Relationship-Based “DIR[®]” Therapy With Older Students with Severe Developmental Disabilities including Autism

Sean Surfas, M.S., Ph.D. Candidate

***Abstract:** Developmental, Individual Difference, Relationship-Based (DIR[®]) therapy, known also as “Floortime” (Greenspan, 1999) has been utilized with young students with developmental disabilities including autism in early intervention programs. The DIR[®] model helps to understand children and families by identifying, systematizing, and integrating the essential functional developmental capacities. These capacities include the child’s functional-emotional developmental level; individual differences in sensory activity, processing, and motor planning; and relationships and interactions with caregivers, family members, and others. The purpose of this study is to ascertain whether or not these methods would also prove useful with older students in secondary programs. This study was conducted over a three-year period, and did suggest that the methods utilized in DIR[®] therapy also proved useful for children between the ages of 12 and 20 years old. Autism is a processing disorder that disrupts the ability to understand and utilize language, organize incoming auditory and visual information, a lack of social interaction and reciprocity, and is usually accompanied by repetitive motor movements, the need for routine and sameness. Because of the ongoing disabling nature of autism, it is of the utmost importance to continue to support the needs of all students with this disability through empirically proven methods.*

Introduction

Over the past decade autism, a severe developmental disability, has seen an increase in numbers and in therapeutic interventions utilized to assist those so diagnosed. Since the definition of autism spectrum disorder was broadened in 1995 increasing the population of individuals with autism, there have also been increases in the number of interventions introduced to the field. DIR[®], also referred to as *Floortime*, a developmental approach designed by Stanley Greenspan, M.D. and Serena Wieder, Ph.D. (Greenspan & Wieder, 1998), increases independently initiated social interactions and social reciprocity. The DIR[®] model helps to understand children and families by identifying, systematizing, and integrating the essential func-

tional developmental capacities. These capacities include the child's functional-emotional developmental level; individual differences in sensory activity, processing, and motor planning; and relationships and interactions with caregivers, family members, and others. Much success has been seen in early intervention programs (Greenspan, 1999; Siegal, 1996) especially with children below the 6 years of age. *DIR*[®] has been used with many different types of children ranging from typically developing to children with severe handicapping conditions. The following study was intended to look at the use of *DIR*[®] methods with older children in order to determine whether these methods are also preferable for older children with autism.

Autism is a processing disorder that disrupts the ability to understand and utilize language, organize incoming auditory and visual information, is usually accompanied by repetitive motor movements, a need for routine and sameness (Siegal, 1996) and significantly poor social skills

The disorder affects the individual with autism's ability to socialize with others in what would be deemed an appropriate fashion. These challenges in language, socialization, and organization are seen in the child prior to age three to rule out other types of development disorders (DSM-IV, 1996). When working with an individual with autism, one must consider the components of the disorder before implementing a classroom instructional program.

A significant part of the disorder is the lack of social interaction and reciprocity displayed by children and adults with autism and mental retardation. Individuals with autism often choose not to interact with others, as it tends to be overstimulating and uncomfortable for them. In other cases, the person with autism may choose to approach another, but as soon as that individual begins to interact with them, they might become disregulated or overstimulated, and rather than display social reciprocity (the back and forth of communications in social interactions) they shy away or become upset. Some children and adults with autism will socially interact, as long as the social connection is one that fulfills a need for them. They may persevere in conversations or fixate on topics, but when the subject is changed, they in turn leave the situation rather than continue the interaction. It is because of this population's deficit in social reciprocity, that *DIR*[®] methods have been utilized.

Problems with social reciprocity has been explored from a number of perspectives¹ and is the focus of a variety of approaches. Koegal and Koegal (1997) discuss that parents deepest concern for their children with autism is to increase their language abilities and social reciprocity. Because 70% of children with autism are

1 e.g. Bauman (1994) in her research at Harvard Medical School has found anomalies in the temporal lobes of individuals with autism. Bauman specifically looked at the Amygdyla and the limbic system. The temporal lobe holds the auditory, memory, and emotional processing centers of the brain. In these areas Bauman and her colleagues found cell volume loss in 244 individual autopsy studies. The particular cell they researched is called the Purkinje neuron. The cell loss in the temporal lobes causes auditory challenges, emotional instability, and memory difficulties.

Courchesne (1991) indicated similar results from his study of the cerebellum. Courchesne also noted anomalies in cell growth. In the case of this study volume density of the Purkinje neuron was noted. Individuals with autism often display proprioceptive (pressure and tactile sensitivity) difficulties.

These anomalies in brain structure, may be associated with overstimulation, disorganization, language, and memory difficulties, resulting in poor social interactive skills and social reciprocity seen in many autistic individuals.

mentally retarded and only 40% use oral language to communicate (Mesbov, 1999), most classes with children with autism emphasize language development as the main use of instructional time (Siegal, 1996). Language development and the use of specific instructional methods, which require significant training, has become the main drive from parent and advocacy groups. A focus on language, however, without a concomitant focus on emotional and social interaction has been a limitation in many programs.

DIR[®], in contrast, focuses on language, cognitive, emotional and social domains and has had a great deal of clinical success with a range of developmental challenges. Because of both rehabilitative and educational philosophies emphasizing early intervention, older children and young adults do not often get the opportunity to become involved in such programs.

Developmental, Individual Difference, Relationship-Based (DIR[®]) Model

DIR[®] is a developmental form of psychotherapy, which works by assisting the child through various stages of socialization leading to higher levels of communication (Greenspan, 1999). *DIR[®]* is used to build social connections and reciprocity between the teacher and student. By building social reciprocity the teacher is able to engage the child at their motivation level to interact in the instructional process. The six stages of *DIR[®]* are as follows:

The first stage of social-emotional development has been termed *Attention and Regulation*- this allows the student to initiate an interaction through eye contact, smiling, cooing, and even crying in hopes of receiving a social connection. Often this may be done to fulfill primary needs.

The second stage of social-emotional development is *Engagement*- this is when the child begins to show an interest and trust in another individual and attempts to communicate with that individual in a way that brings social pleasure to the student. The child responds better to touch, various sounds, and will seek out sensory input, while at the same time being able to recover from emotional distress with the assistance of another.

The third stage is *2 Way Communication*-During 2 way communication the child responds to your gestures, smiles back, frowns back at an individual, and begins to demonstrate the following emotions: closeness, pleasure and excitement from the interaction with another, assertive curiosity, protest and anger in response to the interaction of another.

The fourth stage is *Complex Problem-Solving and Communication*-It is at this stage that the individual begins to close more circles of communication. Circles of communication are closed each time one individual understands the intent of another individual through their communicating modalities. This may be sign language, verbalizations, questions, or movement in space (such as the child that pulls you towards a desired object). For example: An adult asks or gestures to food during snack and the child reaches for the food after nodding that it is the food which he desires. This is a circle of communication.

During these interactions, at least 10 circles of communication must be closed in order for the child to truly be at this level in his social-emotional development. It is

at this stage where the communicative partners begin to share in each other's thoughts and feelings in a fashion that allows for the expansion of play themes, symbolic play, and the beginnings of representational or imaginary play; all which allow for continuing social and emotional growth.

The fifth and sixth stages are called *Forming Emotional Ideas and Building logical bridges between ideas (Logical Reasoning)*: it is during this stage that the child involves another in play themes, simple games of turn taking, communicates wishes by using carrier phrases such as "I want...", and utilizes multiple gestures in a row to communicate ideas. At this point in development the individual closes 30 or more circles of communication during most interactions and more skills for social problem solving can develop.

DIR[®] sessions can take place wherever the child is interacting or existing. The attempt is to use the child's internal motivation to increase his communication, motor planning, and social interaction abilities, rather than depending on adult interaction or prompting. The best use of *DIR*[®] may simply be to help the adult (teacher or parent) learn to interact more often and in a more productive fashion than they usually do with the child.

As part of a special program, forty graduate students were placed in forty secondary educational settings working with children with special needs (especially children with severe difficulties in communication and social interaction). The graduate students implemented a *DIR*[®]-based intervention model with these students (the program will be described in more detail in the Methods section). A few highlights to orient the reader will be presented here.

Brief Excerpts From Teacher Interviews on Communication Patterns Pre-Intervention:

Case #1: Chris

Chris is a 15-year old student who has recently come to the United States from Paraguay and has never had any formal schooling. When his teacher was interviewed in regard to his overall communication and socialization skills the following was reported.

- Question #1: How often does Chris communicate with you now? *Chris has been a little better. He is very sweet. He holds my hand, but does not interact much. Since being in the United States he has watched TV and enjoys Scooby Doo. He likes spiders and the other day pulled me over to the cage and said spider.*
- Question #2: How does he let you know what he needs? *Things he wants he grabs, and he does what he wants to do. He is very difficult to handle when he is in the home center when we are at circle time all the other kids ask me why Chris can move around, play around, and they cannot.*
- Question #3: How does he communicate and interact with his peers? *The kids really like Chris. I have him do calendar and the alphabet every morning (whether he likes it or not). He points with the pointer and repeats after I say the*

months of the year. The kids miss him when he is gone. Chris plays by himself and does not interact with others unless he is brought to them.

Case #2-Ellen:

Ellen is a 16-year old girl with a diagnosis of autism. She is presently in a special day class with kids with various developmental delays. Her parents are actively involved in promoting her welfare. They also were trained in the DIR[®] methods to utilize at home. During classroom activities Ellen stays to herself and does not interact with classroom staff or peers. She has been very aggressive at times, except when she is on the swing; her favorite activity.

- Question #1: How often does Ellen communicate with you? *Ellen is very aloof, but can also be echolalic (repeating back words that are said to her) and does not use words to label objects. She has fun and laughs, but will not engage in conversations.*
- Question #2: How does Ellen let you know what she needs? *She doesn't. If she wants something she grabs it or runs over to it and takes it. If she wants something, and she can't have it at that moment, she will tantrum. Tantrumming has worked for her for years, and I don't see her changing her behavior.*
- Question #3: How does Ellen communicate and interact with her peers? *Mostly she stays to herself unless she really wants to do what someone else is doing. I have never seen her share or have a desire to play with others. If she is not on the swing, then she stays to herself. She will often go and take puzzles that others are working on and fixate on a piece. I don't think her peers like her.*

Case #3-Rosa:

Rosa came to the school three years ago and receives her instruction in both the special and general education settings. Rosa has a diagnosis of moderate mental retardation, but also has suffered abuse and neglect and is currently in foster placement. Her foster parents and teacher report that she is often aloof, and does not enjoy the company of others. Her summer school teacher noted in her cumulative file that she began to whisper words to others, but that she mostly stays very quiet. She has a twin brother who has become very aggressive, as a result of his abuse, and at times takes this out on Rosa. Her guardian noted that she sometimes speaks at home, but very infrequently and it's usually a whisper.

- Question #1: How often does Rosa communicate with you? *Not often at all. She is usually to herself, and appears to frighten easily. She does not trust new people, and will rarely interact with people she does know. She makes no attempt to interact with others, and won't even let us know when she is hurt or bothered by something.*

- Question #2: How does she let you know what she needs? *She does not. She stays to herself and we often have to guess what it is that she wants. We are having to communicate for her much too often. I wish we could get her to trust us.*
- Question #3: How does she communicate with her peers? *Rosa has no friends and only interacts when she is either motored through an activity, or when she really, really likes it. I have never seen her interact with a peer. I think there is someone in there, but I haven't seen her yet.*

Method

Over the three years (three 10-week periods), 40 graduate students began working with students with autism 12 to 22 years of age. The graduate students were all school psychology interns in their 3rd and final year of the program. The student sample (n=40), came from varying schools throughout southern California. The schools were both urban and rural and all the children came from diverse social economic levels. Based on the survey, the ethnic distribution of these students was 35% Hispanic, 40% Caucasian, 20% Asian, and 5% African-American. The majority of students demonstrated mild to severe communication problems. Special day class teachers at the varying internship sites were asked: Who do you find does not engage with others in your class very often? Students were then selected based on teacher nomination. No control group was utilized, as the researchers did not want to exclude any student from a potentially beneficial intervention. The researchers chose to use a waiting list group. This project is considered an introductory or pilot project to determine whether future studies are warranted.

Procedure

The graduate students were broken into three cohorts, each cohort consisted of approximately 12–14 graduate students each of whom worked with one individual. All three cohorts were trained in DIR[®] methods. Though interrater reliability was not measured, the three cohorts consistently demonstrated the knowledge of DIR[®] interventions through clinical experiences prior to working with students in this project. The DIR[®] interventions were implemented over a 10-week period during each of the 1998/99, 1999/00 and 2000/01 school years.

Each graduate student utilized the *Functional Emotional Assessment Scale* (FEAS), a tool designed to include all constructs originally created by Greenspan in his development of DIR[®] model.

An observational rating scale was constructed to determine if the following questions could be answered through the observations of particular communicative behaviors. The survey was designed to provide information that would address the following questions:

1. What level is the individual communicating at prior to any intervention?
2. What level is the individual communicating at after intervention?

This observation approach was used in a clinical form as a way to systematize clinical judgment. It was not intended to be a reliable scale, nor did it have inter-rater reliabilities done on it. Its goal was to systematize clinical observation so that the basis for the students' clinical judgment would be as clear as possible. As indicated earlier, the students were all provided training on the *DIR*[®] model and the interventions that derive from it.

The observation scale consists of 4 areas: (1) Engagement (Self-regulation, interest in the world, and intimacy), (2) Two-way communication, (3) Complex Problem-solving and Communication, and (4) Forming Emotional Ideas. Each area is rated with sub-area contents such as vocalizations, signing, protesting, and other intentional gestures or means of communication.

The observations were rated on a Likert-type scale. There were five levels of observation: (1) A-Ability always present, (2) S-ability sometimes present (3) L-ability lost with stress, (4) N-ability never present, and (5) U-unable to rate. Two points were given for ratings of A. One point was given for ratings of S. Zero points were assigned to any other rating.

Pretest scores were obtained during a 30-minute observation period where the individual was engaged or scheduled to engage in a social activity (playtime, free time, and recreation and leisure times). Scores of the three years were then summed and averaged. After the initial observation, *DIR*[®] therapy began and continued over the 10-week period. Post-intervention scores were obtained during a 30-minute observation period where the individual was engaged or scheduled to engage in a social activity (playtime, free time, and recreation and leisure times). Scores of the three years were then summed and averaged. Statistical comparisons were then investigated.

Results

Table 1: Pearson product moment correlations between Low and Scores at Pre and Post-intervention

Low Score	High Score
*p<.05	.85

Table 1 displays Pearson product moment correlations between the following variables: Low score on the pre and post-intervention and high scores on pre and post-intervention.

Pearson product moment correlations between the following variables were analyzed: Pre and Post-intervention analysis of independent attempts at communication as observed on the FEAS. A Pearson product moment correlation of .85 resulted indicating a strong correlation between low scores at pre and post-intervention and high scores at pre and post-intervention.

Table 2: Mean Comparisons between pre and post-intervention observations

	X	SD
Pretest observations	24.975	12.50
Post-intervention observations	40.25	15.39

Table 2 displays the mean number of independent attempts at communication during pre and post-intervention observation

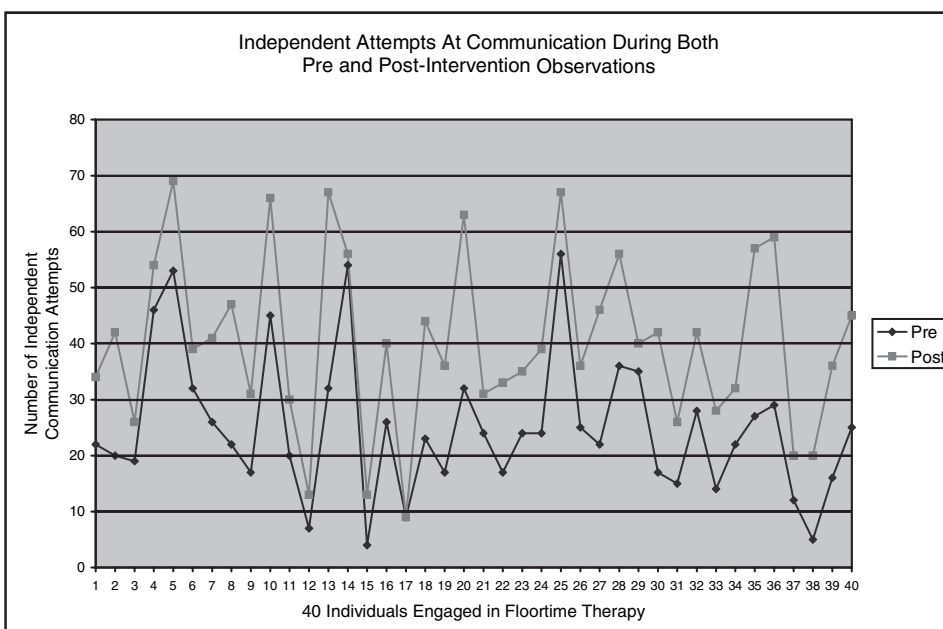


FIGURE 1. displays the raw score values for pre and post-intervention observations of independent attempts at communication.

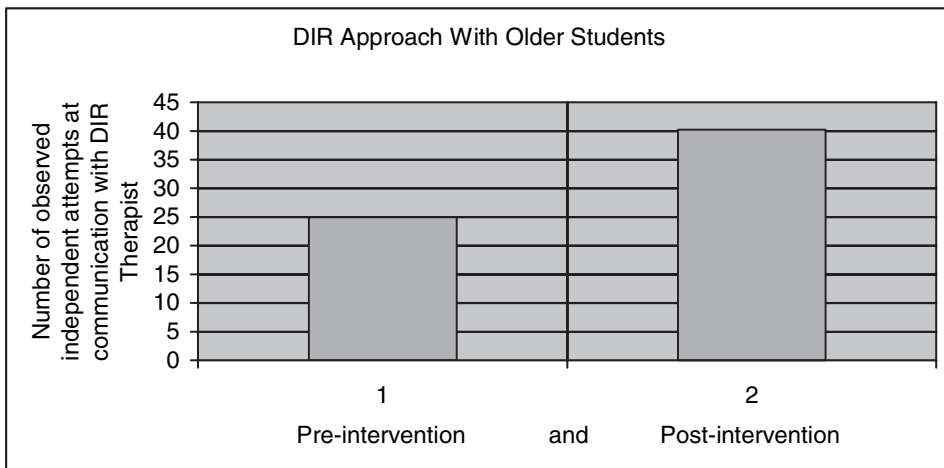


FIGURE 2. displays the mean differences during pre and post-intervention observations of all three groups of students combined.

Test analysis revealed a significant difference between pre and post-intervention observations in their rating on the FEAS observational chart. $T(39) = -11.77$; $p < .001$. (For Pretest $M = 24.97$, $SD = 12.5$; for Post-intervention $M = 40.25$, $SD = 15.39$.)

Brief Excerpts from Teacher Interviews On Changes in Communication Patterns Post Intervention:

Case #1-Chris:

- Question #1: How often does Chris communicate with others? *Since the beginning of his DIR® therapy Chris appears to interact a lot more often with myself and the kids. He doesn't stay to himself as often, and appears to be watching others while they talk to each other and mouths their words. He is a lot more interactive and is trying to use more words.*
- Question #2: How does he let you know what he needs? *Before Chris would pull me to the object or just go and grab things. In the last 3 months he has attempted to name objects (though he is using his own made up words) and point to things more often. We are just beginning to introduce him to pictures for vocabulary building, and he appears to enjoy it.*
- Question #3: How does he communicate with his peers? *The kids really like Chris and miss him when he is not around. I told you that 10 weeks ago, but now they really miss him. They tell him when he is in the wrong spot, and he goes with them now instead of tantrumming. He does not talk back to them, but will smile and watch what they do. He is a pleasure to have in class and now that he is more interactive, the kids just love him.*

Case #2-Ellen:

- Question #1: How often does Ellen communicate with you? *Ellen really seems to enjoy being around others now. We have taken some of her fixation, such as swinging and puzzle piece twirling, and turned them into games for all to play. She will come up and say “puzzle” or “swing” which now means she wants to play with someone. Yes, it is still around her favorite things, however, now she is enjoying being with others. The last three months have changed our outlook on her.*
- Question #2: How does Ellen let you know what she needs? *Before she used to just take things and tantrum when she did not get her way. Now, she loves to say words that people react to. She has just started to say, “swing recess”. This is very important, because in the past it was swing all the time, now she is just recently beginning to realize that swing time will come, but at recess only.*
- Question #3: How does she communicate with her peers? *Ellen still uses only words that bring her what she wants. However, she is able to share more often now, and appears to enjoy just being with her peers. When she would tantrum, they didn’t like to be around her, however now they ask for her if she isn’t here or leaves the room.*

Case #3-Rosa:

- Question #1: How often does Rosa communicate with you? *Over the last 6 weeks it has been amazing. Rosa only whispers a third of the time she used to. She will come up and ask for thing by pointing. She does use a lot of words but she is much more interactive. Other times she waits for me to offer things. If I offer something she doesn’t want, she will shake her head no...she never did that before. It is great to see her interacting.*
- Question #2: How does she let you know what she needs? *She will point to things, but still gives up very quickly if you don’t understand her. She is still not using words, but she will look at you when you are talking and seems more engaged,*
- Question #3: How does she communicate with her peers. *She seems to have made a few friends. There is a little girl that sits on the carpet with her and they smile at each other. Rosa sometime plays with kids at recess, but still doesn’t speak to them. Her foster mother told me that at home she is interacting more often with her home mates, and that she appears happier and smiles like never before. I think the therapy has helped her to trust us, and has helped us to better understand Rosa.*

Discussion

Over the past 20 years, early intervention programs have been a mainstay in the field of special education. Programs such as Head Start and Primary Intervention Programs (PIP) have been used with young children with good results. *DIR*[®] therapy is now being used throughout the Nation with much success. However, it is unfortu-

nate to say that often only the youngest of students (3-6 years of age) are involved in the therapeutic intervention. This study attempted to investigate if the methods described earlier in this article would also be successful with older students. In California, there is a continual increase in the student special education population (OSEP, 1999). Students are not only being newly identified, but many are coming in from other states and countries and require specialized intervention; whether they are 3 or 20 years old. School districts and local regional centers are beginning to identify *DIR*[®] as a viable method to assist these students to increase both social and communicative skills.

Therapists working with the students indicated through both qualitative and quantitative measures that interactions with their chosen student increased dramatically during the 10-week session. The graduate students also revealed remarks made to them by parents and teachers also indicating that they had seen communicative increases in their students and children.

Though this study was only a preliminary glance at whether the methods would work well with older students, all therapists involved indicated that teaching staff would like the sessions to continue as they saw them as benefiting the students. No student was denied entry due to level of intellect or communication ability, however it was interesting to note that all students demonstrated increase in their communication and social reciprocity skills. The study also suggests that students who had some ability to communicate independently, increased their ability to communicate at an even higher-level than students who came to the study without any independent communication ability. This may suggest that all students at various levels of ability can be involved in this type of intervention. Whether they communicate or not is not necessarily the only product of the intervention; social reciprocity and the expansion of social interactions is as important.

Parents reported to therapists such comments as "I have never seen my son so interactive," "my daughter seems to be very interested in what I am doing," and "my kid is playing a lot with his sister." These comments suggest that the *DIR*[®] therapy in which their children engaged helped to increase the social interactions with the challenged student and his respective family members. This is the intent of the therapy and was the subsequent desire of the therapists and investigators in this project.

It is too often the case that only younger students are given intensive intervention, and older students are believed to have plateaued in their skills and that their current skill levels should be accepted. This belief of not being able to teach an older student a new skill was found to be untrue within this study. *DIR*[®] methods assisted 40 students between the ages of 12-20 to communicate with more purposeful intent, and to expand their communications thus increasing their social reciprocity experiences.

As we made clear earlier, an important limitation of this study is the fact that the students did not use a standardized assessment tool (with reliabilities done on it) to investigate change. On the other hand, the behaviors that were investigated were readily observed and quantified (e.g., opening and closing circles of communication). The types of behaviors quantified were easy to observe (e.g., initiation with another person, sharing materials, interactive play with other peers, etc.). Therefore, this study serves as a useful pilot effort, setting the stage for a more systematic investigation of the impact of the *DIR*[®] approach on adolescents and adults.

Summary

The purpose of this study was to see if older students would benefit from the *DIR*[®] intervention. This study suggests positive results that warrant further investigation. It's very important to carry out these additional investigations because, at present, the vast majority of programs focus on vocational skills (with a focus on compliance) for adolescents and young adults with severe cognitive, language, and communication challenges. As we have tried to show, these individuals are capable, with an appropriate program, of improving their social and emotional skills and, through that, their overall adaptation and likelihood of being successful in vocational programs and living arrangements in the future.

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CLINICAL PRACTICE

Articles in this section will include single case studies and descriptions of independent approaches to clinical practice.

Language is More than Speech: A Case Study

Morton Ann Gernsbacher, Ph.D.

***Abstract:** Some individuals face severe challenges with producing oral language (i.e., speech). In this article a case study of a child who experienced severe challenges with speech development is presented. Medical records, historical home videos, audio recordings, and photographs, in conjunction with an extensive journal maintained by the child's mother provide the basis for this report, which profiles the child's development from birth to age 8;0. This child's development demonstrates the necessity of distinguishing between language—the mental representation of concepts and their relations—and speech—one means for communicating mental representations.*

***That the word language derives from lingua (“tongue”) betrays the common confusion about the relation between speech and language.
(Schein & Stewart, p. viii)***

Some individuals face severe challenges with producing oral language (i.e., speech). In this article a case study of a child who experienced severe challenges with speech development is presented. Medical records, historical home videos, audio recordings, and photographs, in conjunction with an extensive journal maintained by the child's mother provide the basis for this report, which profiles the child's development from birth to age 8;0. This child's development demonstrates the necessity of distinguishing between language—the mental representation of concepts and their relations – and speech – one means for communicating mental representations.

Neonatal Development

RH was the first and only child born to middle-age, professional parents. He was the product of an uncomplicated pregnancy, followed by a Caesarian delivery prompted by failure of labor to progress. During labor, RH's heart rate was observed to decelerate rapidly in response to larger uterine contractions. A Caesarian delivery was prepared for, but not executed, earlier in labor because of this precipitous heart-rate deceleration. An eventual Caesarian delivery was uncomplicated, and RH's birth weight was 7 lbs, 7 oz, with Apgar scores of 9/10 (1 min/5 min). RH's immediate postnatal behavior was remarkable, according to his mother, for demonstrating a calm, soothed demeanor, very early and natural nursing (i.e., within moments of being handed to his mother), and striking visual attentiveness. His mother recounts

that he fixated the ceiling mounted television while being held in his father's lap in the hospital bed to watch several minutes of a collegiate basketball game (the Final Four championship).

RH's first months of development were characterized by a calm demeanor, positive affect, and high visual attentiveness. RH began producing a social smile at 5 weeks, 5 days. RH greatly enjoyed leg extension activities, such as infant "kick gyms" (i.e., attractive stimuli dangling within kicking range, when RH was supine) and "Johnny Jump Ups" (i.e., a cloth saddle attachable to door openings with springs that allow an infant to bounce vertically using his legs). RH's mother reported that RH would remain exuberant about jumping in a baby jumper for nearly an hour. RH was also reported to enjoy watching commercial video tapes, beginning as young as two months of age when he primarily watched videos of other baby's faces (producing a range of emotional expressions), and later (beginning in the third month) when he began watching videos of children's educational shows, such as *Barney*. RH was able to sit unaided by his fifth month of life and began crawling at the beginning of his seventh month. Immediately upon beginning to crawl, RH was reported by his mother to cease enjoying the baby jumper.

RH was characterized by his mother and by other adults as a "very quiet baby." He rarely cried and had very limited babble, even by eight or nine months of age. He remained quite happy, playful, and curious, by his mother's report, but did not produce typical amounts of or a typical diversity of vocalizations. According to both his mother's report and recorded audiotape, RH produced little gurgling or cooing, and the sparse babbling produced was primarily vocalic (i.e., produced with vowels, not consonants). RH was reported to experience the onset of "stranger anxiety" at a developmentally typical point (around seven months) and passed the standard "a-not-b" object permanence task developmentally early (Smith, Thelen, Titzer, & McLin, 1999). RH could stand unaided by nine months of age, and shortly before his one-year birthday he began to walk. According to historic home video tape, RH's first succession of more than two steps unaided comprised 16 steps and a half-turn. According to medical records, RH's 'well baby visits' with his pediatrician were annotated with the phrases, "highly social" and "very active" at 6, 9, and 12 months.

Toddler Development

RH's mother reported that by the end of his first year of life, RH was particularly interested in numbers, letters, and colors—all interests that would maintain and strengthen through his second and third years of life. Indeed, prior to his second birthday, he arranged a set of large (8" x 4" x 2"), plastic alphabet blocks in perfect alphabetical order; he arranged correctly the letters in his name using large (12" high) foam letters, and he arranged in numerical order large, plastic numbers 1 through 20. He virtually always alerted to numerical or alphabetical stimuli, and he enjoyed watching videos about counting or spelling, in addition to videos portraying other toddlers or preschoolers playing. He was introduced, by one of his babysitters, to

videos starring the twin celebrities, Mary-Kate and Ashley Olsen, filmed when they were preschoolers, which he greatly enjoyed watching.

As a toddler, RH continued to be characterized by his parents and other care providers as cheerful and highly active, and an additional trait—an inordinate sense of physical balance—became apparent. RH's mother reported that he very rarely fell, despite his interest in walking in precarious environments (e.g., cobble stone streets) and his frequent climbing on furniture and other scalable structures. At 14 months of age, he began a toddler gymnastics program and was distinguished from the other same-aged toddlers by his agility in running quickly, without falling, down a 'tumble track' (a 40' by 10' trampoline). Despite RH's active mobility and agility, RH's mother reported in retrospect that his reaching and grasping were rare. She did not feel the need to remove, for example, fine china displays that were in his arm's reach because he never approached these objects or others with his hands. Materials on kitchen counters, his parents' work desks, or other surfaces that were within his toddler reach were never disturbed. Even earlier, during his first year of life, he rarely reached for anything (a desired toy, his mother's hair, or his father's or other care providers' eye glasses) with his hands. Because manual (e.g., index finger or flat palm) pointing is a developmental outgrowth of manual reaching (Hammes & Langdell, 1981), it is not surprising that RH did not develop or use any pointing behavior during the second year of life.

RH's vocal production remained severely limited during his second year of life; his mother reported, and historic home video suggested, that he was even more "quiet" (i.e., non-vocal) after his 13th month than he had been during the last half of his first year of life. RH communicated primarily with facial and other whole-body nonverbal expressions (predominantly those of positive affect, e.g., joy, satisfaction, curiosity, attention, and on rare occasions those of negative affect, e.g., distress or frustration). RH frequently led an adult to a desired item (e.g., a video) by either taking the adult's hand after RH began walking, or previously, when RH was only crawling, taking the adult's shirt bottom (as RH crawled along). RH's mother viewed this form of communication as highly adaptive for a child whose volitional vocalizations and distal arm and hand control were so limited, and this style of communication remained a core part of his communicative repertoire for several years, becoming more fine grained (e.g., leading an adult by the hand to a door, and then placing the adult's hand on the round door knob that RH was unable to open).

During his second year of life, RH enjoyed viewing visual stimuli upside down and would do so by facing backward to the stimuli, bending at the waist, and looking back at the stimuli between his legs. For example, often when watching familiar videos, RH would face away from the television, bend at the waist, and watch the video inverted by looking back toward the television between his legs. When a small, portable television was placed on the ground, RH stood behind the television and bent over it so that his head rested on the ground, only a couple of feet from the screen, and the image was inverted. RH's mother reported that RH resisted having books read to him, by grabbing the book out of the reader's hands and then studying intensely the bar code of the ISBN on the backside of the book. (His mother

reported that by 30 months of age, he was proficient in bar code; i.e., he could distinguish altered bar code from authentic bar code.)

RH appeared to be fascinated by looking through sheets of colored acetate, and indeed, according to his mother, a sheet of red colored acetate was the first object that he demonstratively shared with his mother, encouraging her (nonverbally) to also look through the acetate. RH's mother reported that RH was also very interested in door hinges, automatic doors, escalators, and the non-right angle caused by the family's vaulted living room ceiling. To this latter stimulus RH would lead his mother and indicate nonverbally for her to observe the unusual angle. RH's mother interpreted this act (RH's leading his mother by the hand to the floor underneath the non-right angle and directing with gaze his mother's own gaze to the angle) as an act of initiating joint attention. However, the communicative act, which RH's mother reported as quite successful, was accomplished without index finger pointing or verbalization.

Given RH's appreciation of visual stimulation during his toddler years, RH's mother reported introducing him to his first computer game when he was 19 months old. RH's parents purchased a child-sized trackball, which used a 4" wide surface and a slow tracking speed. With the child-sized trackball, RH needed to move only his arm, rather than more fine-grained movements of the wrist or fingers, to control the cursor's movement. RH experienced great success with the computer game; RH's parents report that adults who observed him playing this computer-based game would "stand in awe." One game involved a computerized version of a form board for which the child needed to bring the cursor to a puzzle piece and then drag the puzzle piece to the appropriate outline shape. Although at this time RH was completely unsuccessful at putting together even the simplest of physical form boards, he mastered the computerized version instantaneously. Another game was akin to a child's version of a conceptual slot machine. The goal was to click through several different options to select three of a kind. RH mastered that game without any adult guidance. RH's expertise with computer games kept his mother from assuming that his lack of speech was due primarily to cognitive limitations.

RH's stranger anxiety remained during his second year of life, although by all formal measures (e.g., Ainsworth, Blehar, Waters, & Wall, 1978) and informal assessments, RH maintained a secure attachment with his primary care provider. RH's mother notes that he was "less likely to make eye contact" with novel adults than other children his age and that he rarely oriented when his name was called (i.e., made the controlled movement to look up and orient to the direction from which the person was calling). RH's mother reported (and historic home video demonstrates) that RH was unable to follow with controlled vision a directional prompt, such as an adult pointing an index finger to a distal or even proximal stimulus. Thus, RH appeared to lack the traditional markers of receiving joint attention (Tomasello & Farrar, 1986).

After reviewing family photos and historic video tapes, RH's mother observed, in retrospect, that RH must have had extreme tactile sensitivity on the palms of his hands and in and around his mouth. In many photographs he was shown using fist

hands to grab seemingly innocuous objects, such as a soft, rubber therapy ball. In many contexts, he appeared highly reluctant to use his hands for exploration (such as with novel toys and novel food). In one family photograph he was shown retching after being encouraged to touch a “koosh” ball. RH’s mother reported that he was at this point in development highly resistant to having his teeth brushed, wearing hats and gloves (even in the winter), tasting novel foods, and trying on new shoes.

At RH’s 18 month ‘well baby’ visit, RH’s mother expressed concern to the pediatrician about RH’s speech delay. Records indicate that RH’s mother’s concern was not because she and her child could not communicate quite effectively, or that he was unable to communicate with others, but because comparing his expressive language development with typical milestones indicated a delay. RH’s pediatrician recommended an audiology examination, the first of which was conducted when RH was 19 months. According to records, the first behavioral audiology exam was completely unsuccessful with RH failing to alert to any of the auditory probes. Another behavioral audiology examination conducted at 20 months indicated that RH alerted slightly to one or two of the auditory probes; however, the test was far from conclusive. A third behavioral audiology examination conducted at 21 months was equally inconclusive with the exception of RH orienting rather strikingly to the audio track of a Barney videotape, which his mother had brought to the examination and which was presented auditorily at the conclusion of the examination.

At 22 months RH was evaluated via Brain Stem Auditory Evoked Response (also known as Auditory Brainstem Response), while RH was sedated as an outpatient at a hospital. The evaluation indicated no evidence of abnormal neurologic conduction through the brainstem auditory pathways. At 23 months, RH was evaluated by a multi-disciplinary team at a national clinic for developmental disabilities. With the exception of the Bayley Scales of Infant Development (Bayley, 1969), very few standardized tests could be administered, and even the Bayley was an approximation. A highly experienced developmental pediatrician observed and interacted with RH and his mother during a two-hour session. The result of the multi-hour evaluation was a diagnosis of pervasive developmental disorder.

Following this evaluation and diagnosis, RH was enrolled in occupational therapy and speech/language therapy. RH’s parents used as a guide to their interactions the “Communicating Partners” curriculum (e.g., MacDonald, 1987). They reported placing great emphasis on following their child’s lead, reciprocating his interaction, enhancing his strengths, encouraging all of his efforts toward communication (even those assumed by other programs to be ‘unconventional’ or ‘inappropriate’), and sharing mutual affect. In addition, RH began attending an integrated toddler program for two hours a day during the week. A speech-language therapist and occupational therapist were assigned to RH at the integrated toddler program, in addition to those professionals whom he saw in the community; however, after a few sessions with the occupational therapist assigned by the toddler program the parents declined her further services because she used ‘pull out’ sessions with tasks that were too frustrating for RH.

The speech-language therapist at the toddler program suggested developing sign-language, a decision, which in retrospect for RH's mother, seemed ill-conceived. RH's fine motor control was not developed well enough to promote even the simplest of signs. Nonetheless, the speech-language therapist worked for eight weeks with RH on the ASL sign for "more." When RH was unable to produce this sign independently after eight weeks, it was suggested to RH's mother that RH lacked the symbolic understanding needed for "developing language." RH's mother reported that she disagreed strongly with this assessment and asked the staff if they had any evidence that RH was able to produce the component motor plans for the sign (e.g., bring hands to the midline). They did not (e.g., RH had never clapped).

RH's mother later wrote in her journal the following entry related to this topic.

What a bias we as a society have against children who can't talk. This week RH was transitioning to a different classroom with different teachers in a different building at a different time of day. Before he left the house on Monday morning I asked RH if he wanted to take something special with him to school to serve as a transitional object, though I didn't use that term. RH chose two small dolls: one of his buddy, Bert, and the other of his buddy, Ernie [characters from Sesame Street]. As it turns out the teachers took the dolls away from RH, shortly after RH's father left for the day, because the dolls were "commercial." After looking around for them for 10 or so minutes, RH went to the art table and picked up two markers: one yellow and one orange. Because he then carried these two markers around with him the rest of the morning, always setting them down when he was playing with something else, but making sure that they remained with him, I was told on Tuesday during the first parent-teacher conference of the term, that we already had a problem. When I asked what the problem was with carrying around two markers, not even knowing the colors or the fact that the teachers had taken RH's dolls away, I was told that the behavior was 'weird.' Had RH been able to muster even just a "ehhee" or "buh buh" as he made the markers dance in his lap during music time, the teachers most likely would have figured out that RH was demonstrating the highest level of representational play (Ungerer & Sigman, 1981).

Preschool Age Development

According to RH's mother, during RH's preschool years he remained a delightful child, whose mood was almost always "off the charts" in positive affect. He sometimes seemed other worldly and frequently marched to his own drummer; however, he remained affectionate and engaging with persons he knew well, including his immediate family, his other care providers, and the speech-language and occupational therapists in the community with whom he worked after leaving the toddler program. He remained physically active, and he frequently sought out opportunities for proprioceptive feedback (such as jumping on beds and trampolines). According to RH's speech therapist, it was primarily while jumping on a trampoline that RH was able (during much of his preschool age years) to produce the phonation required for any vocalization, which remained quite primitive during this time.

RH developed a relationship with a surrogate sister, a neighbor, who was three years older than he, and with whom he spent one full day a week during the summer

and occasional days during the academic year. For over a year, when RH was 5 years old, he had a same-aged best friend (DW), a typically developing boy with whom RH played one-on-one for about six or more hours a week, always with support. By all observable measures, DW enjoyed RH's company as much as RH enjoyed his. RH taught DW as much about sand physics, water physics, and weather stripping, which was one of RH's fascinations during that period of his life, as DW taught RH about more typical 5-year old boy interests, such as water gun fights and rough housing. RH's and DW's very close bond of friendship appeared to require little speech. Unfortunately, according to RH's mother, the relationship ended abruptly the day that DW—with no malevolence or seeming premeditation—suggested to RH when they were dividing up who would play what that RH play a particular character, because—like RH—that character “would never talk.” RH appeared to be immediately heart broken and despondent, and the bond was never repairable.

RH typically avoided all mutual eye contact with strangers, although for a short period RH adopted the habit of squinting after he made brief eye contact with novel people. RH's fine motor skills remained severely impaired, including the bimanual coordination needed for sign language and conventional gestures, as was his eye-hand coordination. Because RH's manual motor skills were so severely challenged that he struggled to produce common gestures and conventional sign language, RH appeared to create his own gesture system, which drew on motions that he could perform. According to his mother and his speech therapist, RH had a repertoire of a dozen frequently used idiosyncratic gestures and was sometimes able to spontaneously generate novel gestures, which were typically iconic of motions or spatial relations about which RH was attempting to communicate. All gestures at this point in RH's development were produced bimanually. RH's mother reported that most persons not familiar with RH's gesture system interpreted his movements as being repetitive or erratic.

RH was unable to volitionally produce facial expressions, but his repertoire of spontaneous facial expressions was moderately sized. All of RH's vocalizations at this point in development were primarily vocalic; his consonant repertoire was limited to /m/ and occasionally /b/. Many of RH's vocalizations were produced in what his mother referred to as “squeal mode;” however, audio tape analysis demonstrated that many of these “squeals” carried the intonation of well-formed utterances. For example, during one session with his speech therapist, RH vocalized the intonational pattern of “I'm not yawning,” after his speech therapist teased him about looking a bit tired. As with RH's facial expressions and manual gestures, RH's vocal expressions were all spontaneous (i.e., he was unable to produce vocalizations on command or in volitional imitation).

Grade-school Age Development

When RH was 5;5, his mother watched a British Broadcast Company documentary (BBC, 2001) about an Indian mother and son who had worked together to

enable the son, minimally verbal, to develop handwriting as a communication medium; RH's mother then had the opportunity to visit with the mother and son in the United States (Mukhopadhyay, 2000). Although RH's mother was unwilling to go to the extreme measures that the Indian mother had used with her son, RH's mother was very motivated to explore the possibilities of RH using even a gross style of handwriting for augmentative communication. Realizing that RH had less control over the smaller muscles (such as those used during typical-sized handwriting) than he did for larger muscle groups, RH's mother designed a system so that RH could begin by using larger muscles, such as his shoulder girdle. She placed large sheets of easel sized pages on the wall at RH's shoulder height, and RH practiced marking (with a slash) using a wide felt-tip marker in large, designated regions. RH began with considerable physical support (hand-over-hand), which was slowly faded over the course of several weeks.

Once RH mastered the ability to mark independently within a several inch region of a designated target on the large easel-sized paper, RH was able to use this gross style of handwriting to demonstrate his literacy. For example, one of the first exercises accomplished by RH is shown in Figure 1; the goal was to mark through words in a list for which the vowel digraph 'oo' was pronounced /u/ as in "tooth." RH's success on this task demonstrated not only his self-taught literacy, but also his finely tuned phonemic awareness. Another task required identifying the correct verb tense, as shown in Figure 2, and another, as shown in Figure 3, required identifying the correct contraction (and verb tense). RH's mother reported being a bit surprised to observe RH's knowledge of prefixes and suffixes, as shown in Figure 4, in which only one prefix or suffix fits each stem word. RH scored perfectly on each of these activities and many more, all taken from a 3rd grade Language Arts workbook and all completed during the first week after RH mastered a marker, when RH was 5;10.

Upon RH's mastery of using a marker, this ability was used as a communication medium. For example, RH's mother reported that if RH woke up with a fever, she would make a list of body parts that possibly could be in pain (e.g., head, throat, ears). For presumed "yes" or "no" statements RH's mother originally offered only a "yes" and "no" response placed beneath the statement (e.g., "I am hungry. YES NO"). However, RH began sometimes to mark through both answer choices, as shown in Figure 5, and another time RH marked through both answer choices—and made a marking in between, as shown in Figure 6. Then he made only the marking in between the two answer choices, as shown in Figure 7, and RH's mother reported finally understanding his intention: RH wanted a maybe option, which he used in many politic situations, as shown in Figure 8. RH's mother reported that the "maybe" option was quite useful; she recounts an incident in which she was about to become angry at RH for pouring out a container of water she had asked him not to pour, and prior to scolding RH, she decided to find out if rather than RH doing this forbidden task on purpose, it was an accident. His answer was "maybe."

RH continued to use this gross style of handwriting (i.e., marking through options) as a medium of communication for over two years. During that time, RH was able to scale down from the easel-sized pages to more standard 8.5 x 11 typing

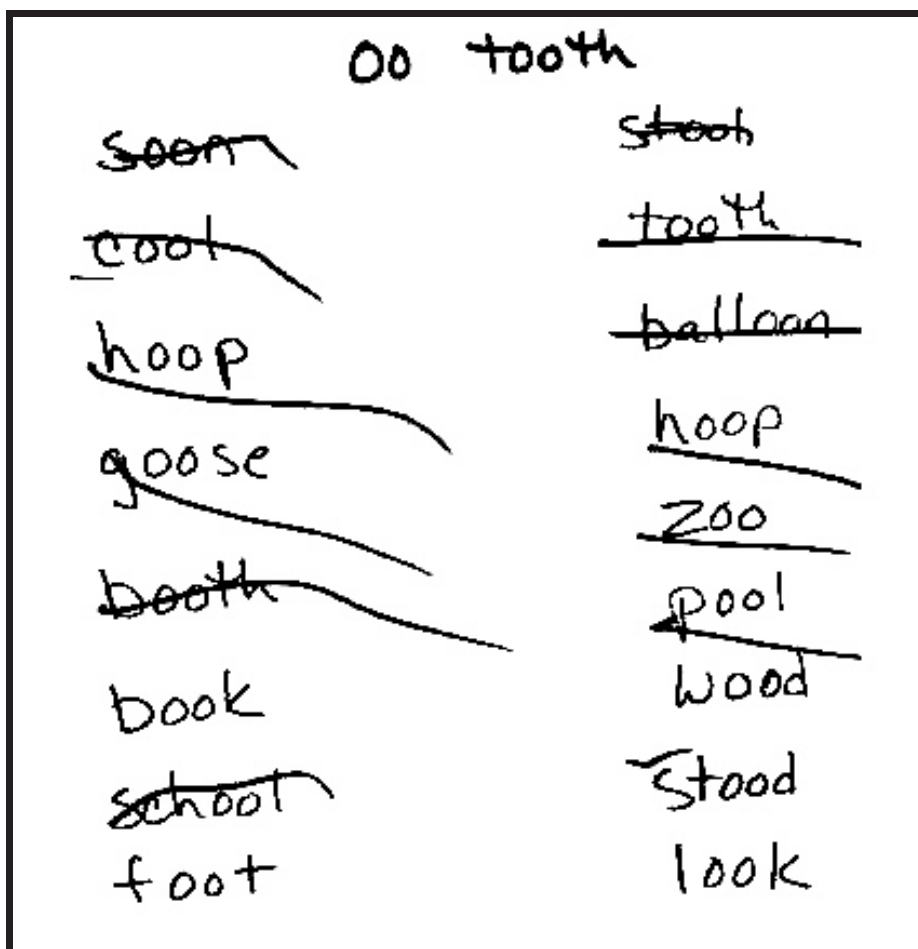


FIGURE 1. Handwriting by RH's mother with over marks by RH.

paper. When paper was not available (or necessary for recording academic work), RH used a magnetic writing toy (e.g., "magnadoodle"), which he carried in his backpack. RH was able to communicate about wants and needs, and to have extended conversations about abstract and complex topics, such as religion, death, and the societal versus medical definition of disability.

Only a few months after RH mastered holding a marker, he was administered the state-wide assessment of academic skills for fourth grade. This standardized multiple-choice test assessed skill in writing, mathematics, and reading, using a multiple-choice format. With the only modification being spacing the answer choices about four inches apart, rather than the mere millimeters that typically separate bubbles on computer-scored answer sheets, RH scored perfectly on the 150-item standardized test. A month later, he scored perfectly on the state-wide assessment for fifth grade. He was 5; 11.

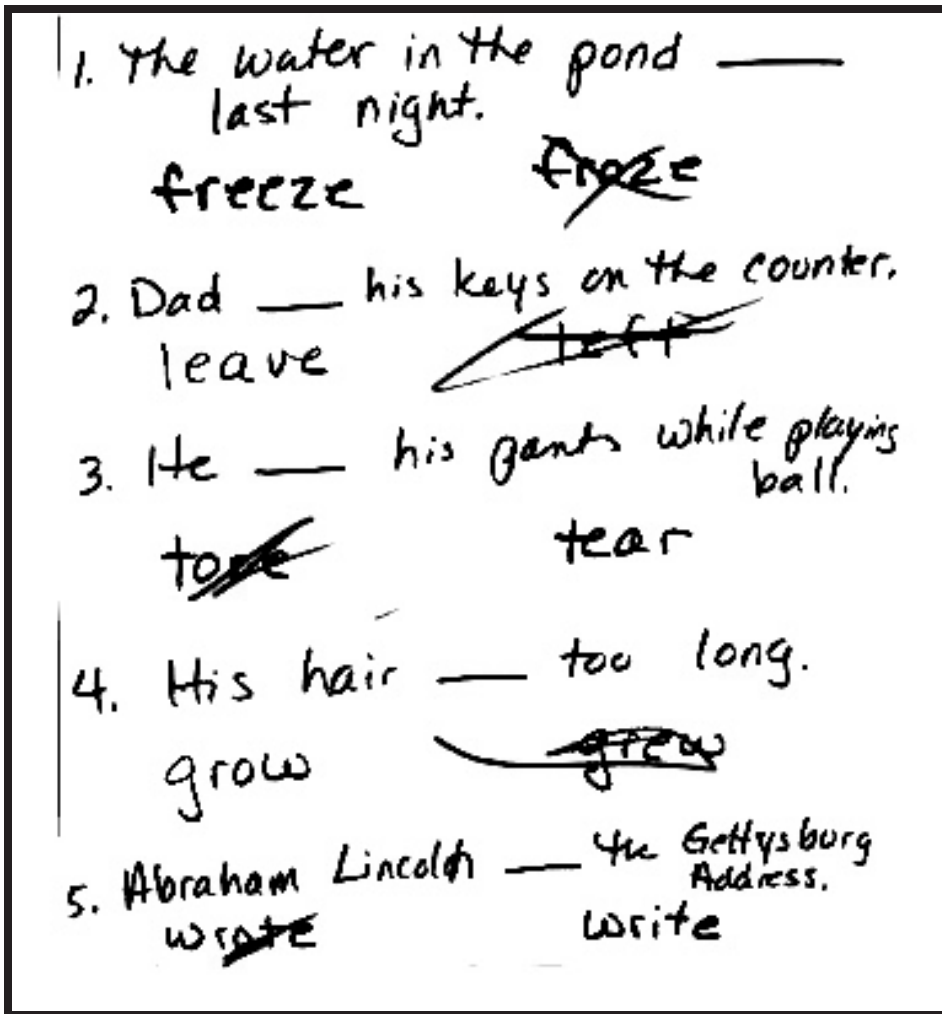


FIGURE 2. Handwriting by RH's mother with over marks by RH.

When RH was 6; 4, he was tested on the Peabody Picture Vocabulary Test (Dunn & Dunn, 1997), a commonly used verbal IQ test. RH would have been untestable with the standard requirement to point to the correct picture, because he still did not have a reliable proximal (or distal) point at that age; however, the picture plates were scanned into a computer, and RH was allowed to use his large, child-sized trackball to scroll to the correct answer. RH achieved a raw score of 181, which translated to a standardized score of 160, at the 99.9th percentile, with an age equivalence of 22 years. Similarly, RH's performance on the standardized Test of Receptive Grammar (Bishop, 1983), in which children select the picture that best represents the sentence, and the sentences vary in their grammatical complexity, was at the 95th percentile. At this point, RH's mean length of utterance (commonly known as MLU) was 1.5, and the intelligibility of his utterances was less than 20% to familiar listeners.

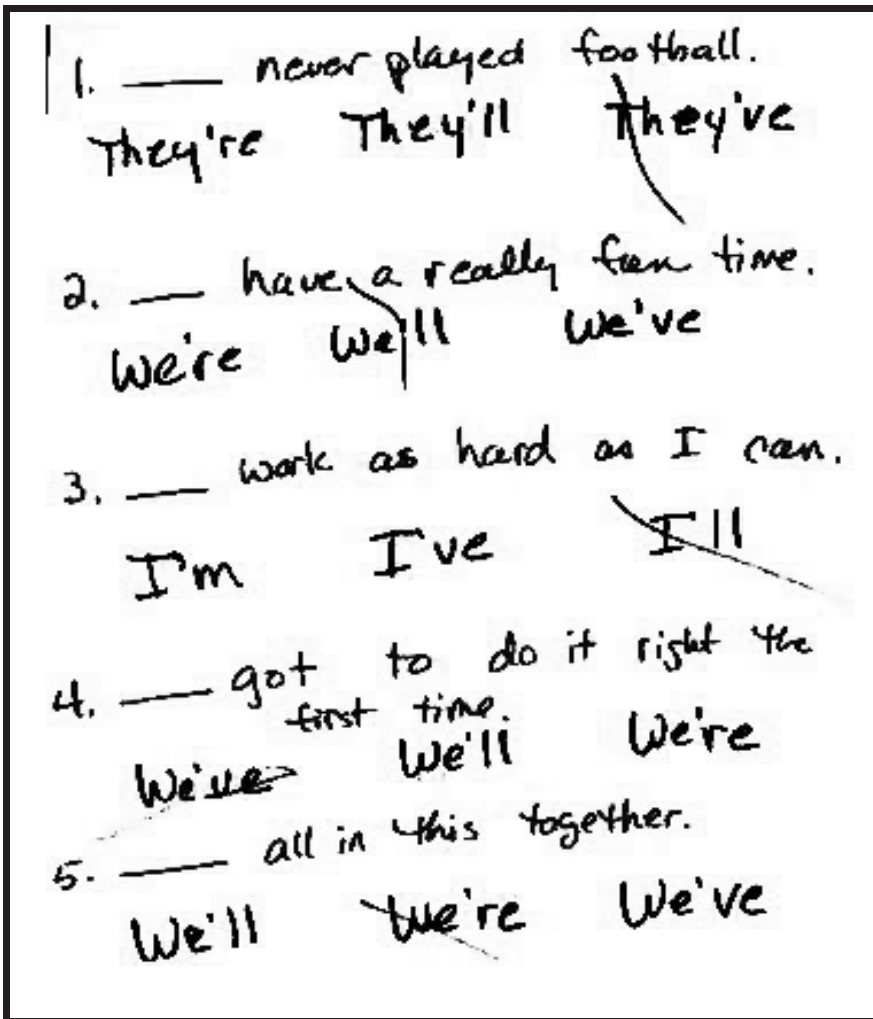


FIGURE 3. Handwriting by RH's mother with over marks by RH.

When RH was 7; 5, he developed a reliable index finger point. His mother reported that this development was a highly celebrated accomplishment; it followed development of his trunk strength and stability, coincident with development of his shoulder girdle strength and stability, and involved a range of finger motility and isolation that RH had not been able to achieve before. Indeed, the isolated index finger point was RH's first uni-manual—as opposed to bimanual—gesture. With his newly developed ability to point, RH and his mother considered whether RH might be aided by using a keyboard type augmentative communication device. They had considered a keyboard type augmentative device three years earlier, before they began the modified handwriting, but RH's body was not ready to support an index finger point at that time.

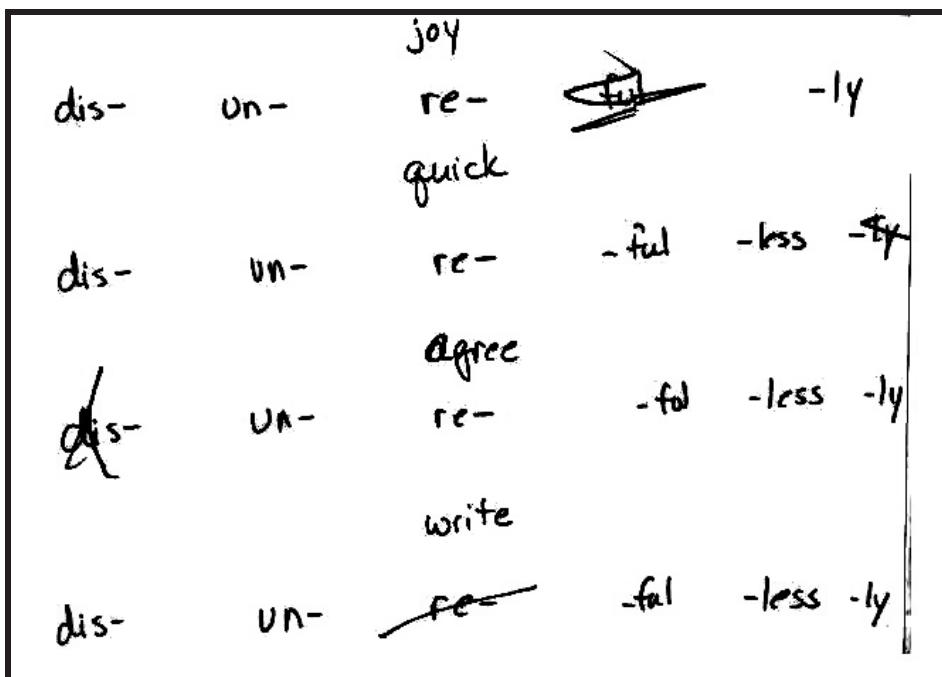


FIGURE 4. Handwriting by RH's mother with over marks by RH.

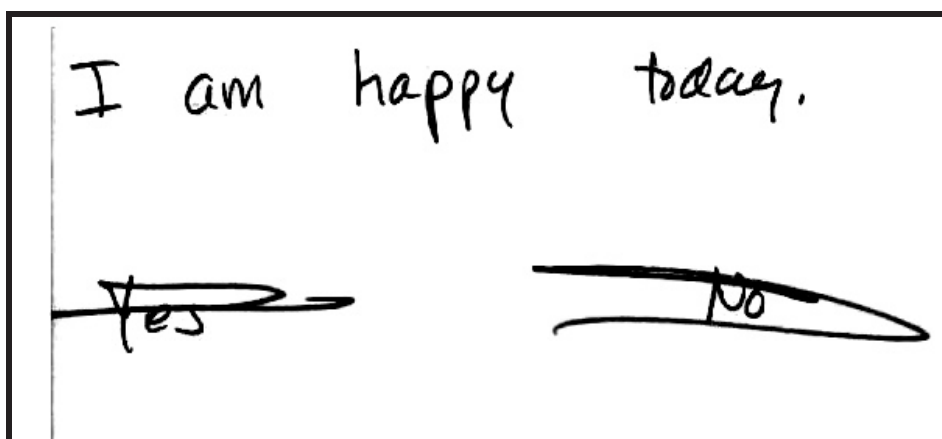


FIGURE 5. Handwriting by RH's mother with over marks by RH.

RH's mother began with the same strategy that she had used with the modified handwriting, namely, starting with an ample-sized target so that RH could use larger muscle groups while practicing to use smaller muscle groups. Thus, she produced a cardboard replica of a QWERTY keyboard with .5 inch-high letters spaced 1.5

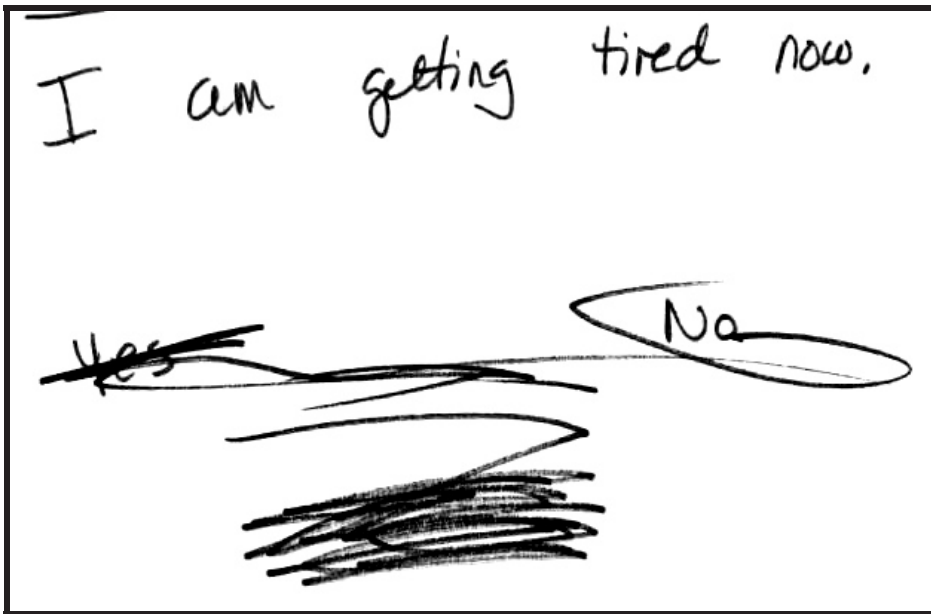


FIGURE 6. Handwriting by RH's mother with over marks by RH.



FIGURE 7. Handwriting by RH's mother with over marks by RH.

inches apart horizontally and vertically. RH began with physical support at the wrist while seated in a person's lap (for further proprioceptive input and support). The wrist support was faded to support at the elbow, and the lap support was faded to sitting beside the person providing support. The elbow support was then faded to a light touch on the shoulder, and then physical support was faded completely. With

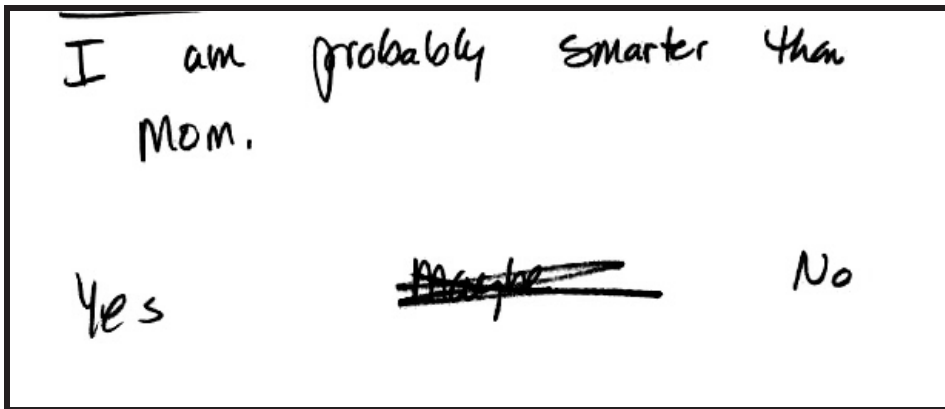


FIGURE 8. Handwriting by RH's mother with over marks by RH

RH's approval, the size of the keyboard replica was reduced two additional times, with the last adjustment approximating the size of a standard computer keyboard. RH and his mother reported appreciating the cardboard keyboard (i.e., the keyboard replica) because it was more portable and more durable; for example, it could be used when RH was in various physical positions, rather than seated with the keyboard on a flat desk-like surface.

As with the gross style of handwriting, which RH had mastered a couple of years earlier, RH also used the modified typing (i.e., index finger pointing to letters on the replica keyboard) both for academic work and for general communication (including email and postal mail, which was RH recorded manually by an observer while RH composed on the replica keyboard and then transcribed to other media). The modified typing demonstrated that RH's language skills included highly advanced expressive language, in addition to his previously demonstrated highly advanced receptive language. The modified typing also demonstrated how naturally and fluently RH could converse interpersonally when the output did not require vocalization.

For example, RH's mother wrote the following entry in her journal.

Just a week after RH began typing, we had the following exchange. The context was that we were talking about how mad it was making me that RH was at risk of ruining some of his videos because he wanted to flip the "lip" of the video off to see the actual tape (the thing I am calling the lip is the part that the video player does lift up, but people are not supposed to). RH had already broken two videos by too energetically lifting the lip up to see the tape. So I was having a pretty motherly moment in nagging him to not do this anymore. Actually I was telling him in no uncertain terms that I wouldn't do it for him because that's his clever way of getting something done if he knows he'll get into trouble for doing it—he coaxes someone else into doing it for him. So I was pretty steamed about this.

RH typed, "BUT THEY ARE MINE." I replied (in speech), "Yes, I know that they are yours, but I'm the one who spends my time and my money buying them." A note here is that RH's video collection, which is quite extensive, is also quite esoteric. I have to really search far and wide for

each one; it's not like going to ToysRUs and picking up what every other child is watching that week.

RH rebutted by typing, "BUT THEY CAN BE REPLACED," to which I replied, "Yes, I know they can be replaced, but that's more of my time and my money to replace them when I don't like your doing it in the first place." Realizing that I wasn't getting very far with my reasoning, I decided to try an analogy. I asked RH if he remembered the beautiful diamond earrings that he and his father had bought me for my birthday, and he typed, "YES." Then I asked him how it would be if I just flushed those diamond earrings down the toilet because, after all, they are mine and they can be replaced, so how would it be?

RH typed, "LAMENTABLE." At this point I was laughing too hard to be mad. And I confess I didn't really know that lamentable was a word until I looked it up later that night in a dictionary.

Later that night I was telling RH that it was definitely time for him to calm down and start trying to fall asleep, but he was still being a bit too animated. I had reminded him several times to calm down. Then I asked him, "Do you know why it's now time to start calming down and trying to fall asleep?" RH typed, "BECAUSE I AM JUST ABOUT TO PISS YOU OFF." So I then asked, "Do you want to piss me off?" And RH typed, "BETTER YOU THAN ME."

RH's use of the slang term, "piss off" prompted a discussion the next morning of slang and curse words, the bottom line of which is that I learned that RH was highly knowledgeable of an entire lexicon of slang and curse words. Indeed, his lexicon surpassed mine. He was also fully cognizant of which words were more slang-like compared with which words were downright verboten in formal company, and he could scale between those two extremes. I found this compelling, because my naïve conception was that children learn which words are taboo and how taboo they are by producing them—often without accurate knowledge of their full taboo status—and being reprimanded. At least that's how I remembered learning where on that sliding scale a few verboten words resided according to my own parents. However, RH had not only acquired an extensive vocabulary of slang and curse words, as he had with non-slang/curse words, he had extrapolated from what was likely very rare instances of each word's occurrence to know the word's shock value.

In addition to using modified typing for direct communication, such as conversations and email, RH also used modified typing for creative expression. At 7; 11, he completed a book of 30 poems. The first poem he typed was the following:

*When winter comes,
And snow has fallen,
Trees are barren no more.
Find me at your door.*

RH also used modified typing to clarify the words he articulated with his speech. An audio recording contained a repeated production of the utterance /KOO ki ki/ ('COO key key'), which RH's mother reported was produced while RH was playing with one of his troll dolls (referred to by his family as a "trollie," pronounced /troli/, rhyming with "holy"). RH typed that the target for this utterance, /KOO ki ki/

(‘COO key key’), was “cool trollie.” Another audio recording contained the production, /ga GA ga ga KI k^l/ (‘gah GAH gah gah KEY kuhl’), which RH translated through typing to be “[I] got the one that’s critical” (said in response to his mother asking if he wanted her to print out any more photographs after she had printed what seemed to be his one favorite). As a final example, an audio recording contained the production, /æ æ æ I i/ (‘aa aa aa EE ee’), for which the target utterance, revealed through RH’s typing, was “that one is so neat.”

RH’s mother reported that RH’s ability to type also facilitated other people’s understanding of some of his other “atypical” behaviors. For example, even though through much of his toddler and preschool years, RH greatly enjoyed placing items and objects in linear arrangements (typically by color wavelength or other dimensions of importance to him), during his eighth year of life, he enjoyed making large piles or “nests” of favored possessions (such as CD insets, DVD covers, video cases, and books). As his mother reported, this free-flowing style was completely at odds with her own penchant for neatness and order. Thus, one morning when his mother was approaching one of his larger “nests,” she began uttering, “you know, RH, what about ...” She reported not getting any further in articulating her question when RH began giggling. To an outsider, one might think that RH was simply emitting some random outburst of laughter. However, when asked by his mother the basis of his laughter, RH typed, “I THINK IT’S FUNNY HOW YOU’RE NOW TRYING TO THINK OF WAYS TO ORGANIZE MY STUFF. GIVE IT UP MOM. IT’S FUTILE.”

Finally, RH’s modified typing provided a mechanism for him to share insights to the origin of his severe speech impairment. For example, when RH was 7;7 and his mother suggested that he try some oral motor imitation exercises, the following conversation ensued (with RH’s contributions being through modified typing and his mother’s, signified by “M” through her speech):

M: How about we try some imitation?

RH: [looks at his mother quizzically]

M: You know what imitation is, right?

RH: YES, IT IS THE HIGHEST FORM OF FLATTERY.

M: Funny. No, seriously, how would you define imitation?

RH: PURPOSEFULLY MIMICKING ANOTHER PERSON’S GESTURES OR BEHAVIORS.

M: Right. So, let’s try some.

RH: BUT IT MAKES ME SAD.

M: Why?

RH: BECAUSE IT’S SO HARD FOR ME TO DO. I CAN BARELY DO IT.

At another point, also during his attempts at oral motor exercises, RH expressed the following frustration, through typing: IT’S AS THOUGH MY MOUTH HAS A MIND OF ITS OWN.

Conclusions

Over 20 years ago, a document prepared for the federal Office of Technology Assessment, stated that “people of all levels of intelligence are found in the population with the inability to speak, which is one of several neurological or neuromuscular impairments. But, only rarely have distinctions been drawn between those incapable of thinking or comprehending and those who simply cannot express themselves. Lack of speech has been confused with lack of language and often been automatically equated with lack of intelligence” (OTA, 1983). The case study presented in this article has presented a profile of an individual whose struggle with speech should neither be confused with a lack of a language nor be equated with a lack of intelligence. Moreover, this case study has identified other challenges to well-accepted equations such as that between traditional manifestations of joint attention (e.g., pointing and following a point) and language development.

RH is clearly not the first individual to demonstrate the folly of equating language with speech. Others in the lay autism literature (e.g., Blackman, 2001; Eastham & Eastham, 1990) have done so before him, and it is very likely that others will continue to do so. These individuals and their lives demand distinguishing between language—the mental representation of concepts and their relations—and speech—one means for communicating mental representations.

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Commentary

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This case study highlighting the distinction between language and thinking on the one hand, and the ability to speak on the other, emphasizes an important point that most clinicians would agree with but can easily get lost during the clinical assessment and intervention process. It points to the need for better methods to understand and determine an infant and young child's level of thinking. Traditionally we've used certain standardized tests to look at verbal and nonverbal capacities. When we see a discrepancy we tend to conclude that a child has cognitive strengths that are not able to be expressed verbally. But these standardized approaches are often not sufficiently usable for infants or very young children. In addition, many young children with fundamental problems in relating and communicating may not be able to cooperate with such standardized approaches even if their age suggests that they are eligible for such an approach.

Gifted clinicians while working with children often are able to tease out the relative strengths in different areas of functioning. In the DIR[®] model we recommend that each processing area; auditory, visual spatial, motor planning and sequencing and sensory modulation, be observed in a variety of contexts. In addition, we recommend that the child's ability to use all of his processing capacities together to negotiate the different functional developmental capacities also be observed and worked with. The child's functional developmental level can be observed and assessed as an overall indicator of the child's level of functioning. A specific challenge in oral motor and speech capacities need not derail this child's overall functional emotional developmental competencies. For example, as Professor Gernsbacher points out in her sensitive and detailed case study, the child was likely involved in representational play showing the ability to use ideas even though he couldn't speak. Later on as he was helped to communicate through typing he was able to more easily show his complex thought processes.

It's not easy, however, to observe level of thinking and the overall functional emotional developmental capacities in a non verbal child. In addition, it's all too easy to compromise one's interactions, (i.e., Floortime approaches) with a non verbal child because one assumes he's at an earlier level of development than is the case. For example, I often encourage parents and therapists to use pictures and written words as part of imaginative play, not just to communicate needs. In this way we can often help the non verbal child become more creative and reflective. If we don't help

the child negotiate all the functional emotional developmental stages they are capable of mastering we may inadvertently contribute to their limitations.

The challenge of working around a child with a circumscribed limitation to help him or her develop their emotional, social and thinking capacities includes children with visual limitations, hearing limitations and other circumscribed motor limitations. In all these cases the key is to work with the child's stronger processing areas to simultaneously strengthen the weaker ones and to master the functional emotional developmental capacities within their reach. We owe a debt of gratitude to Professor Gernsbacher for so vividly illustrating this important principle in her excellent narrative.

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Developmental Pediatric Approaches to Autistic Disorders: Experience and Reason

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Abstract: *Clinicians treating individuals with Autistic Disorders face challenges in the diagnostic and therapeutic realms. Some of these are reviewed along with the importance of defining meaningful phenotypes for the purposes of research studies as well as for constructing meaningful intervention programs. Developmental, transactional approaches integrating evidenced based research with clinical experience which allow for effective treatments for symptoms such as irritability and chronic diarrhea and constipation are described. Promising genomic and proteomic research initiatives are reviewed. The Southwest Autism Research and Resource Center together with the Translational Genomics Institute have embarked on a multi-pronged project looking at differences at the genomic or DNA level, the transcriptome or RNA level and at the proteome level. Inherent in the clinician's role is keeping families and their children with Autistic Disorders central and key to decision making related to their care. Methods of facilitating that process are discussed.*

Clinicians and scientists addressing the needs of children and adults with Autistic Disorders are challenged by the myriad and subtle variability inherent to the disorders along with the veritable explosion of information published relating to clinical presentations, treatment modalities and research studies. The plight of families in this context is enormous. Not only do parents have the formidable challenge of raising a child with a severe developmental disability but at the same time they are faced with confusing and often contradictory professional advice on how best to treat their children.

This article will focus on several current issues. Firstly classification and diagnostic concerns will be addressed along with the importance of recognizing and differentiating possible clinical phenotypes. At the Southwest Autism Research and Resource Center (SARRC) (www.autismcenter.org) a database has been instrumental in being able to identify numerous clinical issues in Autistic Disorders. The biological basis for some of those symptoms is reviewed along with some of the integrative treatment approaches helpful in managing them. The importance of incorporating interactional issues into these approaches is stressed such as those existing between parent and child and, in a larger context, the transaction between the environment and the child's individuality. The promise of genomic research has heartened many families and current efforts in that regard are reviewed. Inherent to

this approach is the importance of keeping families and their children with Autistic Disorders central and key to any proposed intervention and decision making process.

Thinking in regard to the nosology of autism has been advanced by Mary Coleman and others (Gillberg, Coleman, 2001) who underline the importance of referring to children with Autistic Disorders simply as that. Indeed, as we know, children with autism are very different one from another. It is not just a matter of the degree of the severity of the problem at hand, but rather that we now understand that different children with Autistic Disorders likely have completely different genomic architectures, different proteomic expression, and different modes of clinical presentation (Folstein, Roren-Sheidly, 2001). Referring to this complex syndrome as “Pervasive Developmental Disorders” has poorly served clinicians trying to make sense of children’s behavioral and developmental manifestations as well as for the scientists trying to unravel genotypic differences. Consequently the term “autism spectrum disorder,” or ASD entered into popular use. One pitfall with that designation is the implication that the different diagnostic subtypes falling under the ASD umbrella might be simplistically reduced to diagnostic considerations based primarily on symptom severity. For example, verbal capacity, in which the most severe nonverbal child represents one particular disorder and the higher functioning more verbal individual, perhaps one with Asperger Syndrome, the same and that is not necessarily the case. The term “Autistic Disorders” more accurately reflects current thinking gleaned from the explosion of knowledge from genomic studies. There are likely to be between 10 and possibly more than 100 genes involved in autism, each representing, along with a variety of environmental impacts, a veritable host of Autistic Disorders. And, of course, children are different from one another and children with differences are different one from another as well.

Thus there are likely to be many Autistic Disorders and the challenge then becomes defining meaningful phenotypes based on symptoms rather than labels to better enable the search for answers in the genomic, proteomic realm. Delineation of symptom sets such as the extent of stereotypic behaviors, excessive shyness, histories of regression, family histories of Obsessive Compulsive Disorder or for that matter the presence of significant gastrointestinal symptoms, might be more instructive than lumping all children with Autistic Disorder together with an expectation of finding a specific gene or set of genes for that disorder.

The motto of the SARRC is “answering questions and questioning answers.” Founded by two parents and a developmental pediatrician, the initial motivation was to help parents of children with Autistic Disorders make sense of the very confusing and almost always controversial information that they were expected to act upon. In addition, for medical professionals seeing a wide array of children with a variety of developmental issues, the necessity of being able to adopt an integrative approach to practice became both necessary and valuable. By “integrative” is meant a bio-psychosocial model of integrating complementary therapies with more traditional approaches (Rakel, Weil, 2003) along with integrating children’s functional developmental capacities, their different environmental influences, their constitutional make-

ups, and most important, incorporating all that into the family's culture, especially in this case, the culture of autism. In this context "alternative" treatments can instead become "integrative" with more traditional approaches as certainly both can be used together.

SARRC has maintained a database of children with Autistic Disorders, their siblings and unrelated controls. Validity for a questionnaire which forms the basis for that database has been recently presented (Stephens-Groff, Bay, Melmed, 2004), and a copy of it is available from their website. Criteria for entry into the database include a diagnosis by an experienced clinician and for research purposes, confirmation by further testing including the ADOS and the ADI-R (Lord, Rutter, et al, 1989, 1994).

Mining of that database has led to several findings including co-existing biological concerns in that population. The high incidence of gastrointestinal (GI) symptomatology in the children with Autistic Disorders in this unselected population was among the earlier findings emerging from that database analysis (Melmed, Schneider, et al, 2000). Twenty five per cent of the children with Autistic Disorders had chronic diarrhea, and a further 25% of children had chronic constipation. In total then approximately 50% of these children with Autistic Disorders (and some children did have both symptoms co-occurring) have chronic gastrointestinal dysfunction. At the very least and regardless of whatever other clinical implications there might be, the toilet training process is rendered nigh impossible in that context. There are other possible factors which might play a role in any one child's presentation with chronic diarrhea and constipation with one of the most common being chronic constipation leading to a fecal impaction and subsequent leakage of stool around that fecal impaction (Horvath, Perman, 2002; Afzal, Murch, et al, 2003). Other causes might include carbohydrate intolerance secondary, for example, to lactase deficiency that has been seen in 55% of children with Autistic Disorders and GI symptoms (Buie, Winter, Kushak, 2002). Combined deficiency of disaccharidase enzymes is seen in 15% and these enzyme assays correlate well with hydrogen breath tests however the presence of deficiency does not always correlate to any particular GI symptom. Autistic Disorders in and of themselves could pose a risk for nutritional deficiency, e.g., restricted eating habits, pica, etc.

The Opioid Excess Theory (Shattock, Kennedy, et al, 1990; Reichelt, Knivsberg, et al, 1994) has become the basis for one of the most popularly adopted alternative approaches to the treatment of some of the symptoms of autism. This is especially the case when GI problems of the type described are present. Enzymes in the small intestine digest casein, the protein in milk and gluten, the protein in wheat, rye, barley, malt, and oats into peptide fragments, common among them being gluteomorphin, gliadomorphin and casomorphin (Panskepp, 1979; Shattock, Kennedy, et al, 1990). It is postulated that in the case of autism, instead of amino acids, partially digested peptides are absorbed. D'Eufemia and others (D'Eufemia P, et al, 1996) described increased gut permeability, as has Horvath (Horvath, Papadimitriou, et al, 1999). This permeability might allow malabsorption of nutrients, which in turn leads to possible sensitization to those peptides. Once in the bloodstream, the theory is that the peptides might cross the blood-brain barrier and bind to opiate receptors in the brain, possibly leading to irritability and agitation.

The mission of SARRC is to help parents answer the questions they have regarding the rationale and efficacy of these and many other nutritional approaches. Families have told clinicians of the improvements seen in their children following implementation of gluten and casein free diets (GFCF). Previous investigators had identified the presence of peptides in the urine of some children with Autistic Disorders and had used that as laboratory evidence for the justification of the GFCF diet (Reichelt, Ekrem, Scot, 1990). A retrospective look at these peptides in the urine of affected children with Autistic Disorders from the SARRC database, their unaffected siblings and a group of unrelated controls supported the presence of these peptides in the children with Autistic Disorders more so than in their siblings and in typical unrelated controls. It is unclear whether other substances such as soy, bacterial or yeast breakdown products or even endogenous peptides might result in a similar profile. In addition, reports of children with Down's Syndrome also having elevation of these urinary peptides without correlation to aberrant atypical functioning have been published and similarly, children with Celiac Sprue have elevations of these urinary peptides without the presence of autistic symptomatology (Nygaard, Reichelt, Fagan, 2001).

Despite several controversial issues, these findings by SARRC and others (Whitely, Rodgers, et al, 1999) have lent at least some support to what parents of children with Autistic Disorders have been telling physicians for years. As expected, some of these initial reports of improvement were dismissed out of hand especially considering the absence of evidenced based data. However at SARRC once again there was a mandate from parents to try and answer the questions they had while at the same time there was an inherent need to respect parents' experiences and to build bridges in the community spanning often conflicting if not antagonistic practices. Consequently, the issue facing the researchers at SARRC was not necessarily to prove or disprove the efficacy of the diet, but rather to try and come up with a rationale with which to decide who the best candidates for the diet might be and how best to monitor the health and behavior of children who already were on the diet. With that in mind, clinical experience and anecdotal reports suggested that the children most likely to respond were those with a history of multiple ear infections, chronic upper respiratory tract congestion, eczema and unexplained skin rashes, a history of milk sensitivity, as well as GI symptoms such as colic, chronic diarrhea and/or constipation. Also suggestive was a family history of milk intolerance and/or sensitivity. On physical examination findings of a stool mass, sometimes associated with toe walking and posturing was common (Afzal, Murch, et al, 2003). Laboratory findings that might then help support or direct a clinical approach would include the assessment of urinary peptides. Lastly, if the family culture and medical belief system was supportive of the adoption of a complementary treatment modality, there did not seem be any significant harm in pursuing this approach. Of course, it would be appropriate that all children would continue to be followed in medical practices oriented towards emphasizing the critical importance of behavioral and developmental interventions such as would be seen in a typical pediatrician's office. The monitoring of the nutritional status of the child when adopting the GFCF diet is essential and

should include determination of the need for any mineral and vitamin supplementation such as calcium and B vitamins. As in any treatment program, accurate delineation of specific target treatment goals in several domains helps to ascertain the extent to which the diet might be beneficial. Integral to this approach are the wonderful ways in which parents can be supported through acceptance, open-mindedness and with the provision of clinical direction and information. Knowledge is a powerful coping tool but many questions remain.

What kinds of follow-up laboratory studies are needed? What is the role of delayed food sensitivity testing? How can it be determined if this is an effective intervention? A trial of a wheat and milk free diet for a period of three to four months to look at benefits will result in very little harm done. Of course it takes energy, time and money; however the benefits might make the effort worthwhile. Research as to the diet's efficacy in blinded situations is needed and indeed NIH studies have recently been funded looking at precisely that. It is a tough diet to follow, but nonetheless it is certainly warrants closer scrutiny.

Children with Autistic Disorders who have GI symptoms responsive to GFCF diets might well represent a specific subtype of Autistic Disorders. Once again children with autism are different one from another, and delineating those differences will help our understanding of this most enigmatic disorder. In this context caution is also required in the interpretation of treatment outcome studies. If a new antibiotic were to be brought to clinical trial today and all comers with high fevers and sore throats were to be treated with that antibiotic (call it penicillin for argument's sake), it would not pass the muster of a double-blind study, because of course 90% of the children being treated would have viral infections against which penicillin would have no effect. That is the point of sub-typing, genotypically and phenotypically. Conflicting and disappointing results from genetic studies of possible susceptibility genes as well as from treatment outcome studies are possibly a consequence of not stratifying analyses with meaningful phenotypic presentations in mind.

Similarly, the lack of phenotypic stratification might be a confounding variable salient in the interpretation of treatment outcome studies in the utilization of secretin in children with Autistic Disorders. At SARRC several double-blind studies of the use of secretin in Autistic Disorders have been performed and the results of a most recent study have been unblinded and unfortunately there was little good news to report. In that study subjects with specific biological markers were excluded, because it had been determined from retrospective analyses that a more positive response could be expected in subjects without the presence of those particular biomarkers. Nonetheless, again, the findings were negative but there are still those, parents and clinicians alike, who report improvement in various symptoms with intravenous secretin infusions in specific children. If that is indeed valid, it is likely to be the case in a very small subgroup, and certainly not for all children. Trying to ascertain what is different about those specific responders is quite a challenge and hopefully that research will be carried forward. At this point however and until more research is performed, the use of secretin cannot be recommended for treatment of children and adults with Autistic Disorders.

Adults with autism are able to identify social signals more appropriately on faces following intravenous injections of secretin as compared to their abilities on placebo. Simultaneous radiological studies of the amygdala showed enhanced uptake of secretin (Yurgelun-Todd, Rogowska, et al, 2002). Other researchers have emphasized the importance of the amygdala as a component of the neural network underlying social cognition. Baron-Cohen and colleagues (Baron-Cohen, Ring, et al, 2000) have proposed that the amygdala may be responsible, at least in part, for the impairment of social functioning that is a hallmark feature of autism. Amaral reported on the effects of amygdaloid lesions in the macaque monkey that were at variance with this role for the amygdala in social behavior (Amaral, 2003). He demonstrated that the amygdala might not be essential for normal social behavior, as seems to be the case in non-human primates, but rather that damage to the amygdala has an effect on a monkey's response to normally fear-inducing stimuli, such as snakes. These findings suggest that the amygdala has a role in the detection of threats and in the mobilizing of an appropriate behavioral response to those threats, part of which is fear. If the amygdala is pathological in subjects with Autistic Disorders, it may contribute to their abnormal fears and increased anxiety rather than their abnormal social behaviors per se. Regardless of the pathogenesis, does this imply that the use of secretin as a therapeutic modality deserves a further look?

Other novel therapeutic modalities have been evaluated at SARRC. An open label study of the use of oral gamma globulin in a population of children with autism with associated significant gastrointestinal symptomatology has been completed. There has been research into the use of intravenous immunoglobulin on children with Autistic Disorders with the obvious drawback of its route of administration. When oral gamma globulin was used in this open label study, significant improvement in the severity of GI symptoms was seen supporting the possibility that there might be a subgroup of children with Autistic Disorders who have bowel symptoms responsive to oral gamma globulin. Further trials are obviously needed to support these findings (Schneider, Melmed, et al, 2004).

Another set of challenging behaviors in Autistic Disorders include irritability and explosiveness. Is agitation and hyperactivity, in a child of two and a half years with Autistic Disorders a function of disordered emotional capacity? Does it represent a metabolic deficiency or a chemical imbalance? Is it a precursor of ADHD not to mention Bipolar Disorder? Is it rather a function of family stress and lack of coping mechanisms on the part of parents? What decision making process does the clinician have to adopt to come up with a useful intervention plan?

In developmental pediatrics prescription follows description. Once a child is described with both environmental and constitutional factors in mind, a prescription will most often become clear. There are no short cuts. Clearly there are numerous psycho-social factors which need to be considered along with possible biological causes. As an example of that, pain is a common cause of irritability, particularly of nighttime irritability. A child who awakens in the middle of the night screaming, agitated and irritable might have this symptom as a consequence of esophagitis secondary to reflux even with co-existing psychosocial issues. Parenthetically, that might

explain some reports of a subgroup of children with night time irritability being responsive to Pepcid (Lindsay, Tsiouris, et al, 2001).

A popular alternative treatment approach in Autistic Disorders has involved treatment of a host of behavioral challenges including irritability using anti-fungals including orally administered Nystatin. In children with developmental disabilities the measurement of urinary organic acids is primarily used to detect disorders of metabolism with resultant organic acidurias. It has been theorized, however, that certain urinary organic acid elevations might be present that are not necessarily related to inborn errors of metabolism, but rather to metabolic break down products of yeast metabolism. These elevations might be present to a significant degree in the urine of some children with Autistic Disorders, compared to their siblings and to non-siblings controls. In the population at SARRC when these particular urinary organic acids of fungal origin were looked at, aside from elevations in Arabinose, a pentose sugar, no such elevations were consistently present (Schneider, Melmed, unpublished data). One of the issues at hand that loom large in the culture of autism is that those elevations are used as a rationale for evaluating the need for and monitoring of the subsequent antifungal treatment modalities which are being used for a plethora of clinical problems in the alternative community. Their proponents posit that if children with Autistic Disorders have frequent infections particularly Otitis media, and subsequently get treated with repeated courses of antibiotics, that could result in an imbalance of normal gut flora with resultant fungal overgrowth. That in turn might result in yeast infections that could cause irritability and even diarrhea.

For that reason further testing at SARRC was performed by evaluating a series of children with Autistic Disorders to determine the presence of a serum candida immune complex, considered a standard in the determination of fungal infestation. None were positive. In reports from Buie, (Horvath K, Papadimitriou, 1999) no children with Autistic Disorders had evidence of invasive fungal infestations by biopsy nor did any of these children have positive stool cultures for yeast at colonoscopy. In addition, brushings for yeast obtained from small bowel samples were negative. Those findings are further supported from endoscopic studies (Horvath K, Papadimitriou, 1999).

It is certainly unclear as why then there would be any clinical response from the use of antifungals such as Nystatin at all, but it might well be that if there was, it would not necessarily be as a consequence of its anti-fungal properties. Anecdotally reported benefits from its use have included diminished nighttime irritability, improved attention and sleep patterns along with a reduction of tic-like behaviors. The treatment is fairly benign. Little if any intestinal absorption takes place. Tolerability is good with only occasional diarrhea and low-grade fever being seen in the first few days of treatment. Off-label pharmacological treatments including the use of atypical neuroleptics are now more commonly being prescribed for severe irritability and explosive behaviors in the preschool aged population and in that context further consideration for study of the use of Nystatin is warranted.

In Autistic Disorders, co-morbidity is the rule rather than the exception. For example, individuals with Autistic Disorders can have co-morbid ADHD regardless

of their level of functioning (Ehlers, Gilberg, 1993). Clinical manifestations of both disorders have some neurodevelopmental and executive functioning deficits in common. Stimulants and non-stimulant medication have an important role in the treatment of ADHD in this population (Aman, Langworthy, 2000). The use of complementary approaches in treatment has also been described (Levy, Hyman, 2003; Hyman, Levy, 2000) while at the same time further studies are needed to support them. Children with Autistic Disorders are notoriously skittish in their response to almost any medication. Starting low and titrating slowly is certainly recommended. Some children might respond to less than routinely recommended dosages of methylphenidate only to develop significant tolerability concerns at higher dosages. The same is the case for the use of SSRIs such as fluoxetine in children with Autistic Disorders where a positive impact on a child's behavior can often be accrued at very low dosages.

Children with Autistic Disorders are often hypersensitive to sensory stimuli in the environment. These especially include auditory and tactile stimuli but also visual and olfactory stimuli. They can be particularly overwhelmed in highly stimulating noisy environments. Albeit controversial and lacking in strongly supportive data, the removal of what has been referred to as "excitotoxins" (color and sugar, MSG, and chocolate, aspartame) from the diets of children with Autistic Disorders may be an intervention that is possibly of benefit with these types of hyper excitability symptoms. Of course, focusing on achieving a balanced healthy regular diet might, in and of itself, help to alleviate symptoms. Physicians are paradoxical in their attitudes towards dietary interventions. On the one hand when surveyed, physicians generally report a lack of support in their practices for dietary interventions, for example, whether sugar might aggravate irritability and hyperactivity. However when presented with a scenario such as "If a mother of a two-year-old came to your office and described her child as being extremely irritable, hyperactive, and having sleep difficulty, would you recommend limiting "junk food"?", more would say, "Yes, I would do that." Certainly the pragmatism of a practice situation needs to be taken into account.

Anxiety is an often under recognized co-morbid concern. Contributing factors related to coexisting Anxiety Disorders worth exploring might include physical causes such as constipation, diarrhea and pain syndromes. Anxiety can also present with depressive symptoms in this population. Depression in the higher functioning individual with Autistic Disorders can often be related to their feelings of social isolation and rejection. A child with Asperger Syndrome, or high functioning autism, might feel that the world considers them inferior or "dumb". The worst insult for those individuals is to have others disregard them, not take them seriously and not take what they have to say as being important. Individuals with Asperger Syndrome will then keep on talking, belaboring their point, and will use bigger and bigger words, even neologisms, just to let you know that they do know what they are talking about, "so you better listen, and if you haven't got the point yet, I'll continue" type of approach. In that context, when shunned, depressive feelings might arise.

Effective and active integration of children with special needs into the mainstream, such as having typical peers serving as study and play buddies, can be a delightful way to help alleviate anxiety as well as depression. Typical peers are underutilized in their possible roles as peer models and enhancers of appropriate behaviors. Friends in a classroom, out on the playground, and a peer counselor to sit next to at lunch, can all be very reassuring. Even the most aggressive, difficult adolescents will demonstrate some improvement in their behaviors when placed in an integrated, inclusive or mainstreamed classroom, when appropriate expectations are set for them, their typical same-aged peers as well as for their teachers. One of the most important interventions for individuals presenting with depressive symptomatology is to encourage participation in social skill group situations and to have typical peers available to them.

Nutriceuticals as a complementary intervention along with pharmaceutical treatments for anxiety are slowly entering into the therapeutic armamentarium of more traditional health care practitioners. These include the use of minerals such as calcium, magnesium and zinc. Zinc supplementation with concomitant use of psychostimulants has been reported to enhance the effect of those agents (Akhondzadeh, Mohammadi, Hademi, 2004). There appears to be a subgroup of children with Autistic Disorders who have anxiety and attentional symptoms responsive to dimethylglycine (DMG) although well-controlled studies are lacking (Bolman, Richmond, 1999). A study of the use of omega-3 fatty acids in young adults with bipolar disorder showed superiority over placebo (Stoll, Severus, et al, 1999). Studies in children are currently under way. Certainly fish-oil based supplements need to be additive and mercury-free. Several recent reviews of complementary treatments in children with autism and co-morbid disorders are helpful (Levy, Hyman, 2003).

Opportunities for successful integrative therapeutic approaches are ongoing. Fortunately opportunities for developmental progression continue throughout the lifespan. SARRC was involved in the elucidation by Dr Antonio Persico of a possible role for Reelin in Autistic Disorders and that is particularly germane in this regard (Persico, Agruma, et al, 2001). Differences in Reelin gene alleles were found to be a factor predisposing to Autistic Disorders in populations in Italy as well as in Arizona. The implications of this finding are enormous. Knowing that this protein has a role in the layering down of structures pre-natally, and then through the eighth and ninth decade of life, is encouraging as were there to be any therapeutic interventions developed as a consequence of this discovery, then benefit might be accrued for older individuals with Autistic Disorders as well. The importance of this gene in Autistic Disorders has yet to be confirmed; nonetheless the notion that there are developmental genes that continue to have functional expression throughout the lifespan is both hopeful and intriguing. Parents of older children with Autistic Disorders sometimes look on wistfully at the extent of research focused on younger children. What about the teenagers they might ask? And what about the adults? Well, they might be heartened by these findings.

With the advancements spurned from the human genome project, there is now the capacity to evaluate thousands of genes over a relatively brief period of time. It

has been suggested that there might be between 10 and 100 genes or possibly more, involved in autism with several of them interacting in a variety of ways. The expression of these genes results in the production of proteins, which in turn either inhibit or facilitate the production of other proteins. SARRC together with the Translational Genomics Institute, (TGen), have embarked on a multi-pronged project looking at differences at the genomic or DNA level, at the transcriptome or RNA level and at the proteome level. In each strategy, the approach is to compare cases with appropriately matched controls in order to identify one or many genes/transcripts/proteins that are highly correlated with Autistic Disorders. The first prong utilizes linkage analysis in families to examine previously implicated genes in autism for mutations. The second prong looks at both the transcriptomic (RNA) and proteomic aspects of Autistic Disorders. The aims of this part of the study are to compare the level of gene expression in children with Autistic Disorders with those without the disorder. This approach might also allow further insight into the role of circulating toxins or metabolites as a possible trigger for Autistic Disorders. Circulating serum protein markers present in children with Autistic Disorders but not in unaffected individuals that may correlate to environmental exposures are looked at.

The third prong of this collaborative effort is an association study in individuals with Autistic Disorders. Association analysis looks for regions of the genome, which are consistently present in individuals with Autistic Disorders as opposed to controls. This approach will identify both highly penetrant genes as well as more subtle multi-genic interactions. Previous technologies allowed researchers to look on a gene-by-gene basis for problem areas however this and other projects are using technology that can scan up to 1.7 million positions in the genome of each individual, and is thus better able to more readily identify differences in the genomic blueprint between individuals with Autistic Disorders than those without. 1,000 individuals with autism and 1,000 controls are being enrolled in this third phase of the project.

Despite the ability to address these vital issues, a looming problem, which has yet to be adequately addressed, are environmental factors. A gene does not function in isolation. Dr. Greenspan elucidated that a gene functions in the context of a cell, and the cell in context of an organ, and the organ in terms of the body, and the body in terms of the culture, and the culture in the context of the overall environment. Not the least of those environmental issues is the concern regarding neurotoxins. The impact of neurotoxins on the biosphere is huge and the impact of neurotoxins on our child's health is enormous. The Environmental Protection Agency has put us on notice the fact that children are exposed to many environmental toxins everyday, any one of which has myriad possible interactions with another. As much as there is excitement about the genomic revolution, the impact that neurotoxins and possibly even the subtler influence that life experiences have on gene expression is still unknown.

As development is a transactional process, a wide variety of environmental interactive experiences can produce physical changes and visa versa. In order for these forces to be harnessed the decisions of families of children with autism and how they make treatment choices for their children need to be understood and respected. That

way strengths of the families can be harnessed, clearly an essential ingredient in any treatment program. At the same time, by borrowing from the best of what evidenced based and experiential treatment modalities have to offer, the healing capacity of health care providers can be enhanced. Of course, the principle of “first, do no harm” will guide us along this integrative path.

Anyone involved with Autistic Disorders, as a parent of a child with autism, as a therapist, teacher or doctor of a child with autism is entitled to join a very exclusive community. It is a special opportunity. One immediately gets to become a card-carrying member of the family of autism and that is a privilege. Wherever one goes, and whenever one meets somebody else either involved with research or treating autism or is a parent or grandparent of a child with autism, there is an immediate bond established, a bond which transcends national, ethnic, religious, or color boundaries. It is indeed as if one becomes a member of a different culture. However even within that culture there are those who have very differing world views, very different perspectives on what is to be done for autism and why.

If we are to respect family culture as it pertains to issues such as co-sleeping, we certainly need to respect the culture of a family of a child with Autistic Disorders as to how they go about choosing medical care, and how they make choices within that system. It might be appropriate for one family to choose a nutraceutical approach and for another to choose a more traditional route and for a third to choose both. There is strength in that integration

Treatments for Autistic Disorders are neither quick nor glib; the treatment process is simply not a sprint. It is a marathon, relentless and arduous. Having an integrative approach, combining the best of what research and experience have to offer, along with a strong respect for the culture of the family is going to go a long way in helping these children. By respecting the family’s cultural healthcare beliefs, the best opportunity for facilitating the most optimal outcome for the individual with Autistic Disorders is assured. As long as practitioners maintain an open-minded and integrated approach to caring, families can be supported in any situation and with the health practitioner’s sound scientific advice and support, all will benefit.

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Book Review:

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**The Boy Who Loved Windows:
Opening the Heart and Mind of a Child Threatened
With Autism**

Patricia Stacey, Perseus Books, 2003

The Boy Who Loved Windows: Opening the Heart and Mind of a Child Threatened With Autism by Patricia Stacey is a wonderfully rich, poignant book that is compelling and beautifully written. As a parent and a clinician working with children and families on the autistic spectrum I have come to know and work with many children and their families. This book gives a clear picture describing the components that make up autism spectrum and gives hope to all of those who are diagnosed with disorders of relating and communicating.

Ms. Stacey describes what happened with her own son and family in beautiful prose while giving clear, practical information on how to help and work with all children. We need to follow their lead, encourage them to be engaged with us and help them to grow using the developmental model. The method that Ms. Stacey chose to use with her son (Developmental, Individual Difference, Relationship Based-DIR[®]) helped him to engage, attend and enjoy relationships and the world around him.

I find that this book is many things. It is mostly about possibility for change and growth. The hopelessness and despair that parents feel upon having their fears confirmed can be, and often is devastating. When a child is diagnosed with having an autism spectrum disorder it affects the whole family system. In many areas of the country older intervention methods are relied upon and people are not aware that newer methodologies exist-let alone work. Ms. Stacey gives her readers many gifts in her book. She gives clear information on Sensory Integration, Autism Spectrum Disorders, courage and hope.

Ms. Stacey's book is not about shunning the autism community or those on the autism spectrum. Stanley Greenspan, M.D., puts it beautifully when he talks about working with those with communication and learning disorders-"redefining potential". It is about giving hope and help and that there is potential for each child on the spectrum-and that each of us can do better, can climb the developmental ladder and

be more comfortable within ourselves, in the world and with one another. This is the message that comes through in the book and it is an amazing gift to readers.

This book is a must read for parents, family, friends and professionals. Whether you know someone on the spectrum or not, you will gain a new level of understanding on what it is like to live the life of a parent of a child with autism, what a child with autism means to the family and community and that there are wonderful new interventions available to help the child (or adult) to change and grow in a positive way.

NEW BOOKS BY ICDL COUNCIL MEMBERS

The First Idea: How Symbols, Language and Intelligence Evolved From Our Primate Ancestors To Modern Humans

S. I. Greenspan, M.D. & Stuart G. Shanker, D. Phil. (2004)
Da Capo Press.

In the childhood of every human being, and at the dawn of human history, there is an amazing-and until now unexplained-leap from simple, genetically programmed behavior to symbolic thinking, language, and culture. In *The First Idea*, Stanley Greenspan and Stuart Shanker explore this missing link and offer brilliant new insights into two longstanding questions: how human beings first created symbols and how these abilities initially evolved and were subsequently transmitted and transformed across generations over millions of years.

Greenspan and Shanker have formulated a startling hypothesis for which they present compelling evidence-that the critical step in symbol formation, language and thinking is not a “genetic leap” but a learned capacity. That capacity depended on specific types of nurturing interactions and other cultural practices that were passed down and thus learned anew and further developed by each generation, dating back to prehuman and even nonhuman primate cultures.

Drawing on fascinating evidence-not only from their research and collaborations comparing the language and intelligence of human infants and apes, but also from the fossil record, neuroscience, and Greenspan’s extensive work with children with autism-Greenspan and Shanker offer a radical new direction for evolutionary theory, developmental psychology, and philosophy.

The Boy Who Loved Windows: Opening the Heart and Mind of a Child Threatened With Autism

Patricia Stacey, Perseus Books, 2003

In 1997, writer Patricia Stacey and her husband, Cliff, learned that their six-month-old son, Walker, might never walk or talk, or even hear or see. Unwilling to accept this grim prognosis, they embarked on a five-year odyssey that took them into alternative medicine and the newest brain research-and toward a new and innovative understanding of autism. Finally, their search brought them to pioneering developmental psychiatrist Stanley Greenspan, who helped them save their son and bring him into full contact with the world.

This enthralling memoir, at once heart wrenching and hopeful, takes the reader into the life of one remarkable family willing to do anything to give their son a rich and emotionally full life. We follow as they struggle to elicit the first sign that their son is connecting with them, and share in their fears, struggles, tiny victories, and eventual triumphs.

The Boy Who Loved Windows is not only a compelling and inspiring story for parents and professionals who care for children with autism and other special needs, but also a stunning literary debut. It will captivate anyone who cares about the lives of children and the passion of families who put them first against huge odds.

