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Response to Early Intensive Behavioral Intervention for autism—An umbrella approach to issues critical to treatment individualization

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ABSTRACT

Integrating knowledge across the disciplines of genetics, neurological, and behavioral science targets, so far, early identification of children with autism and thus early access to intervention. Cross-discipline collaboration might be substantially improve treatment efficacy via individualized treatment based on the child and family needs, consistency across treatment providers and careful planning of skill curricula, setting and techniques. This paper documents the current state of five main issues critical to treatment individualization where cross-discipline collaboration is warranted: (1) developmental timing, (2) treatment intensity, (3) heterogeneity in treatment response, (4) program breath and flexibility, and (5) formats of treatment provision.

1. Heterogeneity in the autism endophenotype and treatment response

Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders characterized by core deficits in three domains: social interaction, communication, and repetitive or stereotypic behavior, with variable degree of impairment among individuals and impact on affected families.

Is has been suggested that ASD is one of the most familial of psychiatric disorders. Twin studies have demonstrated a high heritability for ASDs around 80–90% (Rutter, 2000). Nonetheless, clinical, and epidemiologic studies suggest that gene penetrance and expression may be influenced, in some cases strongly, by environmental factors (Eapen, 2011). Environmental risk factors perhaps play a role via complex genetic–epigenetic–environmental factor interactions, but no specific exposures with significant population effects are known. A number of endogenous biomarkers associated with autism risk have been investigated, and these may help identify significant biologic pathways that, in turn, will aid in the discovery of specific genes and exposures (Newschaffer et al., 2006). Genetic analyses indicate genetic heterogeneity with considerable overlap with other disorders such as intellectual disability and attention deficit hyperactivity disorder, confirming the documented clinical heterogeneity in symptom expression (Charman et al., 2011) and suggesting simultaneous genetic variations in multiple genes (Dawson et al., 2002; Eapen, 2011). Due to the evident heterogeneity, ASDs are considered as a spectrum of conditions that affect individuals differently, although distinct phenotypic expressions are masked by the limitations of diagnostic symptom representations (Eapen, 2012; Eapen et al., 2013).

Endophenotype research holds considerable promise for the study of gene–brain/cognition–behavior pathways for developmental disorders (Viding and Blakemore, 2006). In the field of ASDs various atypical neurocognitive profiles and neurophysiological alterations that have been obtained from neuroimaging, eye tracking and electrophysiological studies are reported. In early years of life, common behavioral expressions of low-level impairments of social attention and reciprocity are reported: reduced preference and attention to persons and other social stimuli (Klin et al., 2009; Nadig et al., 2007; Osterling et al., 2002; Werner and Dawson, 2005), reduced respond to vocal approaching (Dawson et al., 2004; Klin, 1991; Kuhl et al., 2005; Nadig et al., 2007; Osterling et al., 2002; Werner and Dawson, 2005), poor verbal imitation (Sallows and Graupner, 2005), poor establishing of eye contact (Bedford et al., 2012; Jones et al., 2008; Zwaigenbaum et al., 2005), and recognition of emotions (Oerlemans et al., 2013; Sucksmith et al., 2012). Neurocognitive approaching explored the cognitive–behavioral phenotype and a number of cognitive models of ASD have been proposed over time: the theory of mind-blindness (Baron-Cohen et al.,

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1985; Frith and Frith, 2006), weak central coherence (Happé and Frith, 2006) and executive functions (Ozonoff et al., 1991). To date, few distinct behavioral subtypes have been identified but poorly replicated. Generally, although the total number of factors varied, the majority of studies reported at least one social-communication factor and at least one distinct non-social factor comprising repetitive behaviors and restricted interests (Frazier et al., 2010; Ingram et al., 2008; Munson et al., 2008; Witwer and Lecavalier, 2008). Taken as a whole, the literature suggests that the clinical presentation of individuals on the autism spectrum varies with respect to level of functioning and comorbid disorders (Gadow et al., 2004; Lecavalier, 2006; Leyfer et al., 2006; Simonoff et al., 2008; Witwer and Lecavalier, 2008). Specifically, the proposed neurocognitive models do not seem to be consistently related to measures of symptom severity and social competence (Teunesse et al., 2001) and are appearing on other disorders such as ADHD and intellectual disability (Geurts et al., 2004; Happè et al., 2006; Van Lang et al., 2006). Happè et al. (2006) evidenced only modest correlations between socialization, communication and repetitive/restricted interests and behaviors, suggesting multiple-deficit accounts considering the developmental and dynamic aspects of individual profiles. Thus, do neither account for all characteristic symptoms of ASDs nor are necessarily specific to ASDs. As yet, there is no single theory, which integrates all characteristics of ASD.

The heterogeneity of ASD may not only underlie the insufficiency of single-cause neurocognitive models in explaining the triadic autism phenotype but may also underlie the fast variability in treatment response that is documented in ASD treatment efficacy studies. Meta-analyses and systematic reviews have generally concluded that that Early Intensive Behavioral Interventions (EIBIs) based on the principles of applied behavior analysis appears to be the most effective treatment for ASD to date (Eikeseth, 2009; Makrygianni and Reed, 2010; Matson and Smith, 2008; Reichow, 2012; Reichow and Wolery, 2009; Rogers and Vismara, 2008; Spreckley and Boyd, 2009; Viruès-Ortega, 2010; Warren et al., 2011). Children following this approach demonstrate significant improvements in the areas of autism severity (Sheinkopf and Siegel, 1998; Zachor and Ben-Itzchak, 2010; Zachor et al., 2007; Weiss, 1999); cognitive, language and adaptive functioning (Cohen et al., 2006; Eldevik et al., 2006; Eikeseth et al., 2002, 2007; Howard et al., 2005; Lovaas, 1987; Magiati et al., 2007; Perry et al., 2008; Reed et al., 2007; Remington et al., 2007; Sallows and Graupner, 2005; Sheinkopf and Siegel, 1998; Smith et al., 1997, 2000a), and aberrant behaviors (Eikeseth et al., 2002; Smith et al., 1997). However, although EIBI resulted in improved outcomes for children with ASD applying analysis strategies at a comparison group level, there was a fast variability detected when analysis was conducted at an individual within-group level (Howlin et al., 2009). Therefore, research pointing at factors and methods allowing for treatment individualization is warranted. The crucial question in EIBI research has shifted from general effectiveness toward understanding why outcomes vary across different children and for which children is EIBI most and least effective (Kasari, 2002). Such studies should shed light on which children benefit most from which interventions and the intensity and length of treatment necessary to effect a change. The heterogeneity and developmental nature of ASDs make it unlikely that one specific treatment model or its specific implementation strategy will work for any one child throughout his cognitive and social development. Research points clearly toward the inadequacy of a "one-size-fits-all" approach favoring a single treatment program for all areas of learning in all contexts for children with ASD (Stahmer et al., 2011). Teasing out the active ingredients of effective treatment appears to be fundamental to refinement of strategies and procedures that work best for specific settings, subgroups of children, or providers (Kasari, 2002). This requires an understanding of pre-treatment child and family characteristics as well as specific intervention strategies and delivery formats associated with differential treatment response rates. However, available research provides only limited information on individual outcomes and moderator or mediator variables of the varying developmental trajectory (Lord et al., 2005; Kasari, 2002; Warren et al., 2011). Rates of less than 20% of early intervention articles that measured possible treatment outcome moderators have been established (Wolery and Garfinkle, 2002). Nonetheless, available evidence from meta-analyses indicates a number of predictive pre-treatment child characteristics and specific treatment factors associated with response to treatment. These include larger gains in overall IQ facilitated by higher treatment intensity (Makrygianni and Reed, 2010; Strauss et al., 2013), applied supervisor training (Reichow and Wolery, 2009), and applied parent training (Strauss et al., 2013), lager gains in adaptive functioning facilitated by higher treatment intensity (Makrygianni and Reed, 2010; Strauss et al., 2013; Viruès-Ortega, 2010), inclusion of parent training, higher pre-treatment language skills (Makrygianni and Reed, 2010; Strauss et al., 2013) as well as longer treatment duration (Makrygianni and Reed, 2010), and larder gains in language skills facilitated by longer treatment duration (Viruès-Ortega, 2010). Furthermore, varying strength of predictors has been detected when meta-regression analysis was controlled for subgroup differences between specific EIBI delivery models (Strauss et al., 2013). Specifically, treatment intensity and supervisor training contributed to the efficacy of staff-directed EIBI programs in producing improved IQ and adaptive outcomes, while in contrast, child pre-treatment IQ, language and adaptive skills gain predictive strength the higher the extent of parent inclusion EIBI programs is.

Given the heterogeneity of ASD, EIBI programs, treatment response rates as well as of the strength of outcome predictors, it is likely that a client-centered personalized approach increases a programs efficacy. This requires multi-disciplinary research that is accounting for endophenotypic profiles in explaining subgroup differences in treatment response as well as how behavioral intervention techniques and delivery formats address each of these differences. Such a stance would improve implications for personalized intervention planning as a one-treatment-fits-all approach leads to mixed treatment response, given the many profiles of autism and the differing developmental trajectories individuals may follow. Thus, the following paper discusses a set of issues critical to treatment individualization and thus crucial for any research approach aiming to detangle factors related to heterogeneous treatment response rates and differing developmental trajectories. The set of critical issues – namely that programs that begin earlier, are more intensive, more comprehensive and require parent inclusion lead to better response rates while specific risk patterns of child characteristics lead to non-response – is not exclusive but has been chosen due to the widespread belief in their accuracy. The final goal of this paper is to extract implications from this set of critical issues that allow to modify treatment components in respect to developmental and individual needs, thus to enhance the efficacy of EIBI programs for a wide range of behavioral profiles present in children with ASDs and lately to indicate utile areas where to integrate clinical behavioral and basic neurodevelopmental research, from an integrative umbrella point of view.

2. Critical issues important to treatment response and individualization

A set of critical issues that are widely accepted in their accuracy and appear recurring in the literature – namely that intervention programs that begin earlier, are more intensive, more comprehensive and require parent inclusion lead to better response rates while specific risk patterns of child characteristics lead to non-response