

INVOKING NATURE AND NURTURE IN A SYNERGISTIC TREATMENT MODEL FOR AUTISM

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The worldwide autism community stands ready to “cure” is defined as test scores in the normal range, embrace optimal treatment for these complex neuro- and regular successful school placement and performance (Lovaas, 1987; Rogers and Vismara, 2008). logical disorders that affect an estimated 1 in 44 children according to the CDC (2022). The optimal treatment or treatment package has not yet been identified, but a more powerful synergistic package could be within our grasp today. This rests upon decades of evidence-based research, which provides a set of empirically-based treatment possibilities here referred to as *treatment baselines* or *new starting points*. We now have the opportunity to capitalize here, i.e., build upon what we have fought so hard to learn from both NATURE and NURTURE. Nurture first.

Nurture: Behavioral-Based Treatment

There is strong consensus over the past three decades that behaviorally-based approaches are the gold standard for the treatment and possible “recovery” of young autistic children. Of note, earlier psychodynamic efforts were unable to deliver on their promise (Rimland, 1964). Recovery as opposed to

The two approaches that have most often attained a high standard of success are Ivar Lovaas’ manualized model grounded in learning theory and task analysis (Lovaas 1987, 1993); and Pivotal Response Training or PRT, a Naturalistic Developmental Behavior Intervention (NDBI) that combines key ABA principles and techniques with a child-led developmental approach incorporating motivational variables delivered in naturalistic everyday settings (Schreibman & Koegel, 1996; Koegel et al., 1999; Rogers & Vismara 2008; Uljarevic et al., 2021). Emphases highlight pro-social behavior and initiation, self-monitoring of behavior and self-regulation, and responding to multiple cues in the perceptual field. Though distinctive from the Lovaas discrete trial training approach to teaching, PRT appropriately shares the ABA (applied behavior analysis) designation (Schreibman et al, 2015).

The Lovaas approach aims to teach specific functional skills, reduce problem behaviors, and improve language and intellectual functioning. A step-by-step teaching (didactic) curriculum is prepared for each child and used by the therapists and parents. PRT begins with child choice and uses intrinsic reinforcements to foster child motivation, initiative, and generalization of social communication. PRT has no specified curriculum, but instead involves a set of teaching practices rather than specific teaching content. Each of these Nurture approaches have been fittingly regarded to be “best practice.”

The Young Autism Project

In the early 1970s Professor Ivar Lovaas, Ph.D. of UCLA conducted what later came to be called “The Young Autism Project” across the UCLA, Claremont, and UC Santa Barbara campuses. I had the great privilege of serving as the graduate student supervisor at the Claremont clinic under the direction of Dr. Laura Schreibman, who later went on to develop PRT with colleagues Drs. Robert and Lynn Koegel. At The Young Autism Project we taught children ages 2-4 everything from nonverbal and verbal imitation to a comprehensive array of self-help and cognitive skills; from potty training to story telling and just about everything in between. Children were provided with 40 hours per week of one-to-one instruction distributed between clinic and home sessions conducted by college students and parents. All were intensively trained in the Lovaas mass trial step-by-step curriculum (see Maurice, 1993).

The results, published in the *Journal of Consulting and Clinical Psychology* (1987), were impressive for

9 of the 19 children in the intensive, long-term experimental treatment group. Nearly half (47%) achieved “normal intellectual and educational functioning, with normal-range IQ scores and successful first-grade performance in public schools.” In contrast, only 2% of the similarly constituted control-group children (N=40) met these criteria. “Recovery” or best-outcome status was later replicated for children in Lovaas-styled treatment groups by independent researchers” (Sallows & Graupner, 2005; Cohen et al., 2006).

High Points

- Almost one-half of the children intensively treated “recovered.” *Treatment Baseline*: 47%.
- Acquisition of language and imitation were viewed as “game changers”: levers for at least more normalized development.
- These children were now very unlikely to be candidates for lifetime institutional services costing *far* more than intensive treatment services over a two- to three-year period.
- These very positive findings have been replicated more than once.

Low Points

- A little over half of the children (53%) were “non-responders” in the Lovaas study.
- The successful children were characterized by Lovaas (1994) as “recovered” rather than “cured.”
- The intensity of the program was burdensome for some young families.
- Implementation may be limited by a lack of generalization of acquired skills, high financial costs, and time-consuming nature (Uljarevic et

al., 2021)

Pivotal Response Training (PRT)

The “umbrella review” and meta-analysis of PRT by Uljarevic et al. (2021) states: “Statistically significant effects of PRT were identified across the majority of identified randomized control trials (RCTs) for a range of language and communication skills” (Gengouz et al., 2019). “However, evidence for positive effects of PRT on outcome measures assessing other domains was less robust and/or specific.”

Meta-analysis, albeit limited, has indicated no significant PRT treatment effects for social responsiveness, or for social interaction, or daily living skills (Vineland Adaptive Behavior Scales), overall autism symptom severity, or cognitive functioning (MSEL composite). A pilot study of PRT parent-group training did not find a significant decrease in parenting stress (de Korte et al., 2022).

On the other hand, some studies highlighting increases in self-initiations also resulted in collateral improvements: communication and language, play skills, affect, and reductions in maladaptive behavior (Verschuur et al., 2014). Moreover, recent RCTs highlight increases in expressive and receptive language and adaptive communication skills, and promising findings for cognitive improvement and reduction of overall ASD severity. Mohammadzaheri et al. (2015) reported a significant decrease in disruptive behaviors for PRT subjects even greater than for an ABA group. De Korte et al., (2021) furthermore reported a significant reduction in behavior problems in a PRT group. Minjarez et

al. (2013) indicated a positive impact of PRT training group therapy on stress and empowerment in parents of children with autism.

High Points

- Promotes active parental participation (increasing learning opportunities, treatment intensity, and generalization).
- Recent series of positive findings across multiple dimensions of development and behavior. *Treatment Baseline.*
- Less cost and lower demands on time than Lovaas programs.

Low Point

- No evidence of positive effects of PRT on VABS socialization scores, VABS daily living skill scores, or Social Responsiveness Scale scores.

Nature: Nutritional-Based Treatments

By “Nature,” I refer here to bio-nutritional approaches that have evolved since Dr. Bernard Rimland recommended consideration of Vitamin B6 and magnesium. B6 and magnesium are now only two of many vitamins/minerals believed to promote autistic health and organic recovery. Recovery is thought to center upon healing a permeable “leaky gut” – a dysfunctional, dysbiotic, inflamed “microbiome” tasked to produce about 90% of the neurotransmitters that bear directly upon brain function (the gut-brain axis) (Willett 2023; Svoboda, 2020). Increased gut permeability resulting from maldigestion and malabsorption allows entry of toxins and casomorphins. Protein, fats, and carbohydrates are not properly broken down to be absorbed across the gut wall. Multiple nutritional deficiencies

(e.g., zinc, magnesium, Vitamin B6) are common, and may make it difficult for persons with autism to metabolize and utilize essential fatty acids (Pangborn & Baker, 2005; Russo & de Vito, 2011).

But why turn inward to the gut when we can just “B-Mod” our way out of inappropriate patterns of autistic behavior: correct the excesses, remediate the deficits? Or, “PRT the waters?” Because we can’t! Dr. Lovaas agonized over the 53% that failed to respond even to intensive treatment: “Dean, what keeps me up at night are not my successes but my failures.” Yet Dr. Lovaas looked hopefully to the future discovery of “*the organic variable that is causing the autism*” (1994 interview). If I learned anything from my two pioneering mentors, it was that we must be data-driven. Where we fall short we must be prepared to “try another way” as Marc Gold (1980) reminded us; and honor well established empirically supported treatment – the current APA benchmark.

Bio-nutrition

What we eat matters, or more accurately, whatever you are eating has eaten, matters (Willett, 2023, p. 35) Intake impacts gut-microbiota composition, and even our ability to alter its composition through significant short-term and long-term dietary changes (Wastyk, 2021; Coman, 2020). That is, we can influence our systemic health/brain function by properly, or improperly, feeding gut microbiota. (The Mediterranean Diet gets a very high beneficial ranking (Ristori et al., 2019) while our typical Western diet – high in Omega 6, refined carbohydrates (sugar, flour), additives, processed food – is just... rank.)

For me, the most comprehensive and exciting “Nature” approach comes from Jim Adams and his associates (2018) in their data-driven landmark work. This team carried out a randomized, controlled, single-blind 12-month treatment study of a comprehensive nutritional and dietary intervention. Participants were 67 children and adults ages 3-58 years with Autism Spectrum Disorder (ASD) and 50 neurotypical (NT) controls of similar age and gender. Following a supplement package comprised of 31 vitamins and minerals, Adams and his team sequentially added essential fatty acids, Epsom salt bath, carnitine, digestive enzymes, and a healthy gluten-free, casein-free, soy-free (HGCSF) diet.

Based on blinded clinical assessment, there was a significant pre-post improvement in non-verbal intellectual ability of 11 IQ points in the treatment group (68 to 79) compared to no change in the non-treatment group (86 to 85). Moreover, based on semi-blinded assessment, the treatment group when compared to the non-treatment group had significantly greater improvement in autism symptoms, patterns of behavior, and developmental age. Finally, the treatment group had significantly greater increases in EPA, DHA, carnitine, and Vitamins A, B2, B5, B6, B12, folic acid, and coenzyme Q10. Treatment Baseline.

In an earlier but no less contributory study, James et al. (2004) found that following bio-supplementation, children with autism had significantly altered concentrations of plasma metabolites critical in oxidation and methylation. Methylation is key in suppressing viruses, processing toxins in the liver, controlling inflammation and oxidation, regu-

lating genes, and generating sufficient neurotransmitters in the brain.

Through the oral administration of folinic acid and betaine, and later an injectable form of methylcobalamin, the researchers were able to normalize metabolic imbalance in the autistic children. Of note here is that empirical observations of clinical improvement in speech and cognition have been associated with injectable methylcobalamin (see J.A. Neubrander of James et al., 2004).

High Points

- A comprehensive nutritional and dietary intervention was effective at improving nutritional status, non-verbal IQ, Vineland Adaptive Behavior Scales scores for communication, social and daily living domains, and all five of the ASD/behavioral measures. *Treatment Baseline*.
- Parents reported that vitamin/mineral supplements, essential fatty acids, and HGCSF diet were the most beneficial.
- Targeted intervention was shown to normalize critical metabolic imbalance.
- Compared to either form of the Nurture interventions above, the bio-nutritional approach requires less time, money, and resource availability. Generalization is not an issue.

Low Points

- Some families were inconvenienced by adjustments or departures from a normal dietary regimen; or by the administration of multiple supplements.
- Keller's 2021 review of six RCT studies of the GFCF diet showed no effect on clinician-reported autism core symptoms, parent-reported

functional level difference, or behavioral difficulties.

- A few children in the Adams' report did not readily tolerate aspects of the new dietary/nutritional regimen (e.g., "straight" fish oil – before it was mixed with juice, vitamin/mineral supplements in non-capsule form).

Gastrointestinal Research

A final set of studies focuses on GI disturbances in the gut, and prevalence of GI symptomatology and disease in children and adults with autism. (Cryan 2019) reports comorbid GI disturbance in 70% of children with ASD. This represents another opportunity to evaluate *baseline* benefit from an *organic* point of view.

CDC prevalence data for children with autism provided by Fields, et al. (2020) indicate consistently higher percentages of occurrence of vomiting (3.8% v 1.6%), diarrhea (11.9% v 3.3%), loose stools (16.2% v 5.1%), constipation (28.5% v 11.8%), and pain on stooling (16.2% v 6.5%) for 962 children with autism compared to 1487 control participants ages 2-5 years. This pattern of results was typically even more pronounced when comorbid pica was included as a factor, as also reflected in a large data set provided by Dr. Steven M. Edelson (2020) at the Autism Research Institute in San Diego; and dramatically elevated for autism and pica in adults ages 24-58 residing in a now-closed developmental center (Alexander et al., 2019; 2020). At the developmental center, clients with autism and pica (N=17) averaged 2.88 GI *diseases* compared to 0.53 diseases in an autism-only sample (N=15) , 2.25 diseases for developmentally disabled clients with pica only

(N=16) and 1.31 diseases for a control group of clients with developmental disability only (N=16). Of greatest significance here is a CDC report (Fields et al., 2019) that 23.3% of children on the autism spectrum - nearly one-quarter, exhibit pica behavior, with estimates much higher in some studies of adults (see Kinnell, 1985). *Baseline.* In fact, individuals with both autism and pica disorders may be a phenotypic subgroup the autism spectrum requiring a clinical algorithm for categorization and effective treatment (Alexander et al., 2020).

How does the bio-nutritional approach impact persons with pica or autism and pica? Small - sample studies and case studies - like the comprehensive study by Adams et al., (2019) - lead us to believe we are on the right intervention track. Bugle and Rubin (1993) employed Standard Vivonex to reduce/eliminate pernicious coprophagy in three adults with developmental disability. (Standard Vivonex is comprised of 22 essential vitamins and minerals in a readily absorbable liquid form). Moreover, the Adams' group (2019) reported the complete, durable resolution within a week of severe pica (not further specified) for a 7-year-old autistic child (Case C) placed on the HGCSF (healthy gluten-free, casein-free, soy-free) diet. Pica was attributed here by the investigators to many significant nutritional deficiencies, and possibly a metabolic problem with cobalamin absorption or conversion. Finally, pica (e.g., consumption of bar soap, shampoo) was dramatically reduced, along with other marked patterns of autistic behavior and GI symptoms in an adolescent male on a homeopathic regimen (Alexander & Frank, accepted for publication July 2023). At the same time, this young man has made a series of noteworthy prosocial, adaptive, and educational gains, unexpected given a poor prognosis from early childhood: no speech prior to homeopathic treatment, very little eye contact or family interaction, challenging behavior issues, i.e., a former "non-responder." Diet expanded considerably - from almost wholly chicken nuggets to a range of foods and a willingness to try new foods.

What do we believe is happening here? Harmful bacteria in the gut are identified among the likely chief culprits in autism, pica, and autism/pica. If left unchecked, harmful bacteria can excrete dangerous metabolites that can affect the gut, the brain, and the rest of the body (Pangborn & Baker 2005). On the other hand, beneficial bacteria in the gut, or microbiome, can positively affect body weight, the body's susceptibility to infection, aid in food digestion, produce vitamins, and protect against harmful bacteria. For the young man above, Dr. Frank and I believe we have altered the gut-microbiome/gut-microbiota composition and function, with many correlated benefits (see An, 2019).

There may well be a distinct gut-microbial profile (see Svoboda (2020) and Cryan (2019) in Willett (2023).) In their meta-analysis of nine studies of the gut microflora in ASD and TD (typically developing) children, Xu et al., (2019) reported that participants with ASD had: (a) a lower abundance of healthy bacteria, and (b) a higher abundance of unhealthy bacteria. Other authors (Krajmalnik et al., 2015) also reported a critical lack of diversity in gut bacteria strains. Can we expand the positive correlation between the severity of behavioral symptoms and the severity of gastrointestinal symptoms

(Morais 2021) to include the degree of aberration of microbiota profiles? Can each predict the other?

- Some interventions (e.g., fecal microbiota transplants) have strict cautions.

High Points

- Interventions for rebalancing human and gut microbiota to treat disease have included diet, probiotics, prebiotics, and fecal microbiota transplants. Wastyk et al. (2021) has shown that diets rich in both high fiber and fermented foods demonstrate a profound beneficial effect on both the microbiome and immune status in healthy individuals. The result is improvement in gut-microbiota composition and function.
- New methodologies such as “shotgun metagenomics” (Nirmalkar et al. 2022) tie together research on bacterial populations with microbiota transfer therapy and roles in folate synthesis, sulfur metabolism, and protection against oxidative stress (see James et al. 2004).
- Using the six-item Gastrointestinal Severity Index, Adams et al., (2018) reported significant improvement for the ASD treatment group compared to the non-treatment group on constipation, diarrhea, and stool smell.
- Longitudinal studies *could* help us understand the long-term impact of interventions, especially diet and biotic supplements, on bacteria genera in the gut, and prevalence of pica and GI symptomatology and disease. *Baselines*.
- Parents can help build a database by reporting (e.g., to the Autistic Research Institute in San Diego) changes in patterns of GI symptoms (such as vomiting, diarrhea, loose stools, constipation, pain in stooling) associated with specific nutritional interventions or treatment packages.

Low Point

A Synergistic Approach

Dr. Lovaas (1994) stated: “The average environment, which serves the average child so well, does not provide them (i.e., children with autism) with the structure necessary to qualify as a good teaching or learning environment.” He provided two options: modification of innate or organic structures (through pharmacological, surgical, or *dietary* intervention) and modification through experience in order to make the system capable of acquiring information from the average environment (Lovaas & Smith, 1988). Nature and Nurture. The Adams et al. findings (2018) suggest modification of the *internal environment* that on its own facilitates improvement across many areas of autistic/behavioral, intellectual and adaptive, and gastrointestinal function. Yet if both the internal AND the external environments can be conjointly modified, why not aim to “restructure” both together? Could we then anticipate developmental acceleration and behavioral improvement?

Another window into the internal environment has opened recently through “precision nutrition.” This is “the use of the gut microbiome as a biomarker to generate *personalized nutrition interventions* – to seize upon the microbiota to design precision-tailored, individualized dietary interventions (Mills 2019b; Coman 2020)...Precision nutrition through the microbiome offers individuals huge potential to manage disease risk through diet and microbiome-modulating interventions and, thus, improve both

quality and longevity of life (Mills 2019b)."

Dr. Frank's meticulous use of homeopathic remedies individually tailored over time to our clients' core autism symptoms fits this type of precision model (Alexander & Frank, 2023). (See also "Precision Medicine" in Beversdorf 2022.)

We have a wealth of data referred to as baselines or *treatment baselines* here as "*new baselines*" for possible synergistic comparison. Some of this data has already been subjected to separate evaluation. In addition to measures associated with intensive early behavioral intervention, we have research on comprehensive nutritional and dietary intervention; and small-sample (case study and single-subject design) treatment of comorbid autism and pica. Some of this data has yet to be examined through the lens of scientific analysis – e.g., interventions designed to impact bacterial taxonomies. New bacteria-directed technologies will no doubt facilitate investigations of metabolic pathways and improve gut health. But on a still more encompassing stage is the possibility of combining biologic (Nature) and behavioral (Nurture) technologies synergistically. Can we boost the Lovaas success rate from 47% to 75% or better? The gain in IQ scores from 25 to 30 or more points? Can we observe developmental and medical improvement even in those not considered "successes"? Can we witness a decreasing prevalence in pica and GI symptomatology over time across participant groups, and also for individual children in case studies and parent communications to information-gathering agencies? Either the Lovaas or PRT programs may be enhanced nutritionally. Isn't a synergistic treatment package of the

best Nature and Nurture therapies what each parent would want for his or her child? We have empirical starting points to determine if such an effort is a "game changer." Got *Treatment Baselines*? Yep!!

Choosing Options

This paper puts additional options on the table for both the autism field in general and specifically for parents and their children on the spectrum. A sound recommendation made by Lord and her associates (2005) is to start simply and inexpensively. This translates to single-subject and detailed case study rather than group design. If, for example, PRT was initiated across several subjects, and bio-nutrition then introduced at staggered intervals (multiple baseline across subjects), we might expect yoked gains. This may be especially true in *treatment baseline* areas where PRT has been shown to be less impactful (e.g., social responsiveness, VABS daily living skills) and bio-nutrition significantly impactful. That is, if the synergistic hypothesis bears out, we would hope to see time-sensitive accelerated developmental rates.

It is important to keep in mind here that superimposing one approach upon another is different than simply combining a number of applied techniques into an eclectic mix. A bio-nutritional "internal" approach, and an "external" teaching approach – either Lovaas or PRT – operate from different premises. Other treatment models support combining treatments. To illustrate, private practice therapists have long recognized that the best clinical path forward is often psychiatric medication together with counseling/therapy. Such fruitful treatment packages suggest we consider reaching across different parts of the whole child or adult through both

If we have as yet to identify the “cure” long hoped for, our synergistic use of individually tailored options should engender optimism in this first half of the new millennium.

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