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Friends Not Foes: Combined Risperidone and Behavior Therapy for Irritability in Autism

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Challenging behavior often requires a multi-faceted treatment approach. The notion that only medication or behavior therapy would maximize treatment of all irritable, autism-affected youth is simplistic. Yet, individual treatment remains the standard of practice in many settings, with clinicians relying on their most familiar tool. This trend is not surprising because the substantial literature on the effectiveness of behavioral intervention in treating irritable/aggressive behavior in autism^{1,2} has not been well advertised outside of the intensive behavioral intervention community. Nor has this work been shaped into a delivery system that would be suitable for less intensive outpatient settings. Similarly, the literature demonstrating efficacy and effectiveness of atypical antipsychotic is relatively recent and more familiar to psychiatrists than behavior therapists. New innovations are always slow to diffuse initially.³ The time has come to merge these distinct literatures and investigate the power of combined treatment approaches, particularly given the severity of challenging behavior and functional impairment observed in these youth.

In a previous issue, the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network reported an advantage for combined risperidone and parent training in behavior therapy - relative to risperidone alone - in improving compliance and decreasing irritability in youth with autism.⁴ In the current issue, the RUPP Autism Network extended this work, demonstrating improvements in adaptive functions (primarily socialization and communication) with combined treatment.⁵ Together, these reports highlight the potential utility of combined treatment in improving not just irritability, but, more broadly, the functional independence and quality of life of individuals with autism. Although replication and extension of this work is important, clinicians who treat these patients would be wise to consider a combined approach, especially in situations where previous attempts at individual pharmacologic or behavioral treatment have been ineffective. Collaborating with community resources will be essential in settings where both components are not readily available.

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The RUPP study also highlights the need to focus on optimization rather than improvement in this population. Even infrequent or episodic aggressive or self-injurious behaviors can lead to restriction of the individual's access to their social or school environment. They can also result in families feeling anxious and unsafe and decrease the quality of life of caregivers and other family members, who often restrict their functioning in anticipation of the next episode of challenging behavior. While clinicians and caregivers may be excited by observed decreases in challenging behavior, clinical experience teaches that individuals with even low rates of these behaviors remain impaired; and these individuals may be more likely to experience future exacerbations. Completely extinguishing challenging behavior may reduce the likelihood of recurrence because the individual is no longer receiving reinforcement from the behavior. Absence or very low rates of challenging behavior should be the primary outcome in future therapeutic intervention research in this population.

As with many seminal treatment investigations, the RUPP risperidone and parent training study leaves more questions than answers regarding optimal treatment delivery. Perhaps the most immediate questions are: 1) whether there are "subtypes" of youth who benefit from only one form of treatment versus those that require combination treatment? and 2) whether these subtypes can be reliably predicted so that treatment can be tailored from the outset? Many cases of autism with irritable, aggressive behavior show a mixture of biological and environmental determinants, and the precise mixture varies greatly across cases. For example, in clinical practice, youth with a long-standing reinforcement history maintaining their challenging behavior are common. These youth may exhibit aggression or self-injury to escape from overwhelming sensory situations or other demands, to get attention from peers or parents, or to get something they want. In some of these cases, direct behavioral intervention or parent training alone extinguishes the behavior. In others, behavioral treatment alone - even intensive treatment - is not completely effective. This is particularly true for individuals who show a consistently irritable mood. Behavioral treatment alone also tends to be less effective in youth who show no clear behavioral function and youth with a bipolar-like phenotype that includes cyclicity of mood, sleep maintenance issues, or even frank mania.^{6,7} Youth with the latter phenotypes and no clear behavioral function may benefit most from medication only approaches, while youth with behavioral and biological contributions may benefit most from combined treatment.

The strong efficacy of antipsychotics suggests that a proportion of youth may be effectively treated on medication alone, but very little is known about how to predict responders. In behavioral intervention, younger children with developing communication skills and high baseline rates of aggressive behavior driven by escape, attention-getting, or tangible functions may benefit from a relatively short course (~100–200 days) of intensive behavioral intervention.⁸ In contrast, older youth with longer histories of irritable, aggressive behavior may improve slowly but reliably on combination medication and intensive behavioral treatment. More data are needed to determine whether these patterns hold up and to examine whether predictors of medication response can be identified. Identifying robust medication responders will be particularly important as these individuals may be optimized on medication only and would provide the lowest return on investment for adjunctive, resource-intensive behavior therapy. Even if "subtypes" of responders to specific interventions are difficult to reliably identify, an iterative assessment approach that includes

expert consideration of behavioral and biological determinants of challenging behavior should be used to determine the initial treatment approach with subsequent modifications based on ongoing assessment and response.

Another important question raised by the RUPP study concerns the optimal delivery mechanism and dosing for adjunctive behavior therapy. Direct behavioral intervention can be very effective.⁸ However, direct intervention is costly and may be impractical or unavailable in many situations. In the RUPP study, small-to-medium incremental effects were observed using a more portable outpatient parent training approach based on 12–15 (75–90 minute) sessions and up to four boosters delivered over the course of 24 weeks. The enhancement of parent training over medication alone in this study is impressive given the less-intensive nature of the behavioral approach. This begs the question of whether outcomes would be further enhanced by including additional parent training sessions and home visits. What is even more striking about the RUPP results was that the advantage of combined treatment occurred in the presence of a lower risperidone dose. Could more intensive parent training, possibly coupled with direct intervention sessions, further reduce medication dose and limit exposure to side effects? Reduction of medication exposure is crucial in these youth who are often taking multiple medications for autism-associated comorbidities (sleep difficulties, attention problems, seizure disorder, etc.).⁹

The RUPP study design included several interesting advancements beyond standard outpatient parent training, including home visits and booster sessions. It will be important to determine whether these time-intensive, but potentially invaluable, enhancements are essential treatment components. Could tele-health monitoring approaches that involve ongoing, frequent feedback augment the treatment effect at lower cost? Enhancements to caregiver training are a worthy focus of future investigations. Given the influence of managed healthcare and soaring costs, next generation studies should focus on developing the most cost-effective approaches that still optimize treatment.¹⁰ This research can include effectiveness trials that attempt to tailor treatment based on baseline clinical characteristics and functional behavioral assessment.

The RUPP study group should be commended for their strong efforts to bridge the medication/behavior therapy divide. The results provide needed clinical guidance and provoke future investigations to ask practical questions regarding the potential additive or synergistic effects of these treatments are needed to further clinical practice and, more importantly, the lives of these vulnerable individuals and their families.

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