

Pilot Data Supporting Omega-3 Fatty Acids Supplementation in Medicated Children with Attention-Deficit/Hyperactivity Disorder and Deficits in Emotional Self-Regulation

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To the Editor:

RECENT WORK HAS demonstrated that individuals with Attention-deficit/hyperactivity disorder (ADHD) are at elevated risk for deficits in emotional self-regulation (DESR) (Surman et al. 2010). DESR traits include low frustration tolerance, impatience, quickness to anger, moodiness, and being easily (over)excited to emotional reactions (Barkley 2010). Research also suggests that changes in DESR may not routinely follow changes in ADHD symptoms during treatment trials (Shaw et al. 2014). Despite the link between ADHD and DESR, little has been completed in terms targeted treatment trials of individuals with ADHD who manifest DESR.

Although limited, the literature suggests that omega-3 fatty acids (FAs) supplementation may have a modest impact in the management of severe mood dysregulation (Osher et al. 2005; Wozniak et al. 2007). To this end, we examined the effectiveness and tolerability of adjunct omega-3 FAs for the treatment of DESR and ADHD symptoms in children with ADHD who were treated with stimulant or nonstimulant medications and who continued to manifest clinically significant DESR.

This was a 12-week open-label pilot study of omega-3 FAs in children 6 to 17 years with ADHD who were receiving stimulants and/or nonstimulants and continued to manifest prominent DESR. We utilized a target dose of 975 mg EPA. The fish oils were Ω -3FA ProOmega Junior (by Nordic Naturals) with each batch purity confirmed by a certificate of analysis. Individuals with a T score ≥ 60 on the Emotional Control subscale of the Behavior Rating Inventory of Executive Function-Parent version (BRIEF-P) (Giola et al. 2000) or T score ≥ 180 on the 41 questions that make up the Anxious/Depressed, Attention Problems, and Aggressive Behavior subscales of the Child Behavior Checklist (Achenbach and Rescorla 2001) were defined as sufficiently moody for study inclusion.

All analyses were intention to treat with the last observation carried forward. Response was defined as categorization on the Clinical Global Impressions (CGI)-Improvement scale of “much”

or “very much improved” (i.e., CGI-I ≤ 2). Paired *t*-tests compared pre- and post-treatment scores. All tests were two-tailed, and significance was determined at $\alpha=0.05$ (*p*-values between 0.05 and 0.1 were reported as *trends*).

Our pilot sample included seven subjects who completed the study and three subjects who finished study measures through week 6 (total, $n=10$). Of the three who dropped the study, reasons included scheduling difficulties, lack of efficacy, and precipitated anxiety unrelated to medication. The mean age was 10.6 ± 2.6 years, 60% were male, and all were Caucasian. The sample was highly comorbid with autism spectrum and anxiety symptomatology.

In general, there were improvements in DESR, but not ADHD, between baseline and endpoint. Mean CGI-DESR severity scores were significantly different from baseline to study endpoint (4.6 ± 0.7 vs. 3.0 ± 0.9 ; $p < 0.0001$). Similarly, by CGI-improvement for DESR, 70% ($n=7$) of subjects responded favorably to treatment. We did not find a significant change in the BRIEF-P emotional control subscale (65.3 ± 10.2 vs. 58.4 ± 13.0 , $p=0.22$). Only a minority of subjects were labeled as “responders” by CGI-I at endpoint for ADHD (10%, $n=1$), major depression (30%, $n=3$), or anxiety (30%, $n=3$). There were nonsignificant improvements in both dimensional (e.g., ADHD RS) and categorical (e.g., CGI-I/S) proxies of ADHD response.

Comparing baseline to endpoint T scores for the major indexes of the BRIEF-P, we found *trends* to improvement on the Global Executive Composite (73.8 ± 9.4 vs. 65.4 ± 15.2 ; $p=0.07$), Behavioral Regulation Index (72.8 ± 10.9 vs. 64.5 ± 15.5 ; $p=0.08$), and Metacognition Index (72.0 ± 8.4 vs. 64.1 ± 14.5 ; $p=0.07$), suggestive of improvements in overall executive functioning. The majority of DESR responders were positively impacted by the third week of the trial.

Our findings derived from omega-3 FA supplementation to ADHD medication in children with ADHD and DESR showed relatively rapid improvements in mood (DESR), but few improvements in ADHD symptoms. The omega-3 FAs were well tolerated. These pilot data with a nutraceutical provide encouraging

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support for a larger controlled trial of omega-3 FAs as adjunct therapy for residual DESR in treated ADHD youth.

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