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ORIGINAL CONTRIBUTION

Omega-3 supplementation, child antisocial behavior, and psychopathic personality: a randomized, double-blind, placebo-controlled, stratified, parallel group trial

Adrian Raine[1] · Annis Lai Chu Fung[2] · Yu Gao[3] · Tatia M. C. Lee[4]

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Abstract

While some RCTs have observed efficacy for omega-3 supplementation in reducing antisocial behavior, the role of psychopathic personality and gender in moderating treatment outcome has not been examined. This study examines whether omega-3 supplementation reduces antisocial behavior, and whether any treatment effects are a function of gender and psychopathy. Three hundred and twenty-four schoolchildren with a mean age of 11.9 years were randomized into 3 groups: omega-3 ($N=108$), placebo ($N=110$), and no-treatment controls ($N=106$). Parent and child reports of child antisocial and aggressive behavior and psychopathic-like personality were collected at 0 months (baseline), 6 months (end of treatment), and 12 months (6 months post-treatment). A group × time × gender interaction ($p=.016$) indicated that only females in the omega-3 group showed a significant reduction in antisocial behavior 6 months post-treatment compared to baseline ($d=.35$), whereas the females in the two control groups showed no change over time. A group x time x psychopathy interaction ($p<.006$) was also observed, with psychopathic personality levels moderating treatment outcome. Children in the omega-3 group with high (but not low) psychopathic-like personality showed significant improvements in child-reported antisocial behavior at the end of treatment ($d=.19$) Results suggest that omega-3 supplementation may be helpful in reducing childhood antisocial and aggressive behavior in females, and those with psychopathic-like personalities.

Keywords Omega-3 · Antisocial · Aggression · Psychopathy · Randomized controlled trial

Introduction

There is growing interest in nutritional supplements as an adjunct therapy for treating antisocial behavior. This interest is in part stimulated by long-standing research showing that poor nutritional status is a risk factor for externalizing behavior problems [1, 2]. Omega-3 has been hypothesized as one nutritional component that might explain the link between poor nutrition and antisocial behavior [3]. Correlational research has also shown that fish consumption has been negatively associated with cross-country homicide rates [4]. More recently, randomized controlled trials (RCTs) have shown some evidence for the efficacy of omega-3 supplementation in reducing antisocial behavior [5, 6]. One recent meta-analysis on the efficacy of omega-3 supplementation on aggressive behavior from 30 intervention studies reported an overall effect sizes of $d=0.20$, 95% CI 0.14 to 0.26, arguing that omega-3 can successfully reduce aggression and may be a viable intervention [7].

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✉ Adrian Raine
araine@sas.upenn.edu

Annis Lai Chu Fung
annis.fung@cityu.edu.hk

[1] Departments of Criminology, Psychiatry, and Psychology, University of Pennsylvania, McNeil Building, Room 483, 3718 Locust Walk, Philadelphia, PA 19104-6286, USA

[2] Department of Social and Behavioural Sciences, City University of Hong Kong, Hong Kong, China

[3] Department of Psychology, Brooklyn College and the Graduate Center of the City University of New York, Brooklyn, NY, USA

[4] Laboratory of Neuropsychology, The University of Hong Kong, Hong Kong, China

One significant gap concerns the role of gender in moderating treatment outcome. Most prior studies in the antisocial literature have not examined its role in moderating treatment outcome. This is despite the fact that gender differences in the neurobiological consequences of omega-3 and treatment outcome have been identified in other fields. Sex differences have been reported in the influence of DHA on anti-inflammatory processes in the brain, together with gender difference in omega-3 levels in the cerebral cortex [8]. Women show greater improvement in insulin resistance in response to omega-3 supplementation compared to men [9]. Whether sex differences emerge in the outcome of antisocial behavior, however, is currently unknown and requires clarification.

A further significant gap in this body of research is that nutritional RCTs to date have not assessed the moderating effect of psychopathy on treatment outcome. For non-nutritional interventions, there are conflicting views on this issue. One systematic review has documented that in 7 out of 15 treatment studies, children with psychopathic-like traits had *worse* outcomes for antisocial behavior, with 7 more of these studies showing null effects [10]. Another review of treatment studies concluded that 90% resulted in *poorer* treatment outcomes for psychopathic-like children [11]. In contrast, another comprehensive review has argued that despite the pessimism surrounding the treatability of these children, some studies show that psychopathic-like children show improvements in antisocial behavior comparable to low-psychopathy children [12]. A further review of eight treatment studies has concluded that six of these show treatment benefits for psychopathic-like youth [13]. Furthermore, it has been argued that most studies assessing whether psychopathic-like traits moderate treatment outcome have not employed an RCT design, and without such a design, true moderation cannot be tested [10]. As such, against the backdrop of this conflicting literature, it remains an open question as to whether non-nutritional treatment programs can be effective in children with psychopathic-like traits. Whether omega-3 in particular can benefit these children is an entirely unanswered question. However, given the strong heritability for child psychopathic-like behavior [14], the notion that nutritional supplements which act on the brain could benefit such children is not out of the question.

The primary aim of this study was to assess the efficacy of omega-3 supplementation in reducing antisocial behavior in a community sample. From a cross-cultural generalizability standpoint, based on prior findings from Western and East Asian countries, it was hypothesized that omega-3 supplementation would reduce broad-band antisocial behavior irrespective of psychopathy grouping in this East Asian population. Secondary and more exploratory aims of the study were to assess the moderating influence of gender and psychopathy. Since it has been argued that the most persuasive evidence will emanate from studies with an RCT design that tests for moderating influences of psychopathic-like traits and which also utilizes a treatment-as-usual group design [10], hypotheses were tested using an RCT design with intention-to-treat analyses which included all participants and both a no-treatment control group in addition to a placebo-control group.

Method

Trial design

The design consisted of a randomized, double-blind, placebo-controlled, stratified, parallel-group trial (1:1:1 ratio) of school-children. Children with a mean age of 11.89 years (SD 2.59) were randomized into three groups: Controls ($n = 106$), Placebo ($n = 110$), and Omega-3 ($n = 108$) and were assessed at 0 months (start of treatment), 6 months (end of treatment), and 12 months (follow-up). Trial design remained unchanged throughout the study.

Participants

Eligibility criteria

Participants consisted of 324 community-dwelling children and their primary caregiver (104 Controls, 101 Placebo, and 97 Omega-3). Children had to be aged between 8 and 18 years, willing to participate in an RCT, and residing in the community. Exclusion criteria consisted of: (1) allergy to fish or fish products, (2) significant use of fish oil supplementation in the past six months, (3) history of epilepsy, (4) intellectual disability, (5) taking medication that may modify lipid metabolism in the past 3 months. Written informed consent was obtained from the parents, while assent was obtained from the child. Ethical approval was obtained from IRB boards at both City University (Hong Kong) and also the Research Grants Council (a government body in Hong Kong).

Reviews of RCTs have commented that median sample sizes in RCTs are relatively modest, with estimates of 46, 54, 65, and 80 from different reviews [15], and which also characterize omega-3 RCTs of psychopathology [16]. The median sample size of prior studies on aggression is even smaller ($n = 22$; [17]). We consequently aimed for a larger study to detect a small effect size (see below).

Study setting and location

The study took place in rooms at two schools in Hong Kong, from February 2015 to July 2016 and also a research laboratory at the City University, Hong Kong. The study was registered in ClinicalTrials.gov (NCT02334098) under the

title "Omega-3 Supplementation and Behavior Problems" at https://clinicaltrials.gov/ct2/show/NCT02334098.

Omega-3 intervention

Omega-3 supplementation

This consisted of a 200 ml drink (Smartfish Recharge). The base drink in both treatment and control conditions consisted of fruit juice from apple, pear, pomegranate, aronia, and passion fruit. It also contained vitamin D3 (5 µg) and antioxidants (ferric reducing ability of plasma value of 0.71 mmol/100 g). For the treatment condition only, a total of 840 mg of omega-3 (300 mg of DHA, 300 mg of EPA, 180 mg of alpha-linolenic acid, and 60 mg of DPA) was added to the base drink. Placebo drinks were matched exactly with the fish-oil drink in terms of size, appearance, and flavor.

This drink was chosen because: (i) it contains an appreciably higher dosage of omega-3 than standard capsules in a relatively small liquid quantity (60.6% of the size of a standard can of cola) suitable for child consumption, (ii) the fruit-flavored drink may be better tolerated and result in higher compliance with children than standard capsules, (iii) an emulsification process is used in the manufacture of the drink that greatly minimizes oxidation and thus effectively eliminates fish taste and after-taste, helping to keep participants blind to group membership.

Treatment duration and administration

Treatment duration was six months. This duration was chosen to match that used in our prior studies [5, 17] because prior treatment studies have usually been 2–4 months [16], and because a somewhat longer treatment period may be more effective in producing longer-term brain and behavioral change. The omega-3 drink was administered on the morning of each school-day by a research assistant, and by parents on weekends and school holidays.

Demographic variables

Demographic variables were ascertained from an interview with the primary caregiver as follows: sex and age of child, mother's education (graduation from high school), father's education (graduation from high school), residence (living in public housing or poorer), and family income (less than HK$15,000/month).

Outcome measures

The pre-defined primary outcome measures were parent- and child-reported antisocial behaviors, including antisocial personality and aggression. A total of seven sub-scales were translated into Chinese and completed by both parents and children. All instruments were translated into Chinese and back-translated into English by the second author and checked for accuracy by the first author.

Reactive-proactive aggression questionnaire (RPQ)

Children completed this self-report instrument which yields scales of reactive, proactive, and total aggression [18]. Reliability and validity have been documented [19–21].

The antisocial process screening device (APSD)

Parents and children completed this 20-item scale which assesses child and adolescent psychopathic traits [22]. Items are coded 0 (not at all true), 1 (sometimes true), and 2 (definitely true). It consists of three subscales to assess callous-unemotional traits, narcissism, and impulsivity. Overall reliabilities have been reported as good with the exception of the callous-unemotional scale, with good support for the three factor model [23].

Conduct and oppositional defiant disorder scales (CODDS)

Parents and children completed this 23-item measure which is modelled on DSM 5 and assesses the 8 DSM oppositional defiant disorder criteria and the 15 conduct disorder criteria [6]. Each item is assessed on a three-point scale (never, sometimes, often), with items summated to yield conduct disorder and oppositional defiant disorder scores. Good construct validity for these scales have been documented [17, 24].

To both provide more robust indices of antisocial behavior and to help reduce Type 1 error, all child- and parent-report scales were separately factor analyzed to produce two overarching measures (child-report and parent-report) of antisocial behavior using principal component analysis (see below).

Blinding success/failure

In order to assess the degree to which double-blinding was successful, both children and parents in the two drink groups were asked at the end of treatment (6 months) to guess which group they believed they were in (placebo or omega-3).

Side effects

At the end of treatment both children and parents were asked to list any negative reaction experienced by the child that they believed to be a consequence of taking the juice drink.

Sample size

Based on the results of a meta-analysis of omega-3 treatment studies of antisocial behavior, a small effect size of $d = 0.20$ was anticipated [7]. The final total sample size of 324 would have power of 0.80 to detect a small effect size of $f = 0.136$, alpha = 0.05, critical $F(4,642) = 2.39$.

Randomization and stratification

After giving informed consent, participants were randomized into treatment, placebo, and control groups. Urn randomization [25] was used for group assignment, stratifying on age (bands 9–10 years, 11–14 years, 15–18 years) and sex. This stratification procedure aimed to balance groups on key demographic variables.

Adherence to protocol

Adherence to the treatment regimen was assessed on each school day for each child. The research assistant who administered the drink completed a drink consumption log sheet each school day, while on each weekend day this log sheet was completed by the caregiver. These data were used to calculate total number of drinks consumed in the 6 months. Participants were incentivized to comply with the treatment regimen by being offered a meal coupon each month based on the number of drinks consumed. Details on adherence to the treatment regimen are provided in Table 1.

Blinding

In this double-blind trial, all persons involved in data collection and outcome reporting, including participants and their parents, were blind to omega-3 group allocation. Allocation concealment was maintained by having the omega-3 intervention allocation conducted separately by the project coordinator who was kept independent of participants, investigators, and knowledge of which drink codes were omega-3 or placebo. All research assistants who assessed antisocial behavior were also blind to group membership. Coding of the drinks was kept only by the collaborator at an overseas site who had no contact with study participants and was not involved in data collection.

Statistical methods

An intention-to-treat (ITT) design using all randomly assigned participants without any exclusion was employed for all data analyses, with data missing due to loss at follow-up handled using mixed effects modeling [26]. An ITT approach was adopted because it is considered a gold standard method-of-choice for RCTs, is endorsed by CONSORT, respects initial randomization, and provides unbiased estimates of the effect of treatment assignment on outcome

Table 1 Demographics, baseline externalizing behavior, perception of group assignment, and treatment adherence data together with statistical comparisons for intervention groups

	Controls ($n = 106$)	Placebo ($n = 110$)	Omega-3 ($n = 108$)	Statistic	p
Age	11.81 (2.56)	11.90 (2.50)	11.97 (2.57)	F = 0.09	.92
Sex					
Male (*N*)	74	66	69	$Chi^2 = 2.30$	.32
Female (*N*)	32	44	39		
Family income	35.8%	33.6%	41.7%	$Chi^2 = 1.60$	.44
Public housing	49.1%	43.6%	45.4%	$Chi^2 = 0.66$	.72
Father's education	46.2%	43.6%	48.1%	$Chi^2 = 0.45$	.80
Mother's education	45.3%	44.5%	37.0%	$Chi^2 = 1.84$	.40
Child report					
Antisocial factor	.09 (1.00)	-.07 (1.02)	-.02 (.98)	F = 0.70	.50
Parent report					
Antisocial factor	.14 (1.03)	.01 (1.03)	-.14 (.92)	F = 1.99	.14
Assignment perception					
Believed assigned to Omega-3	–	76.0%	72.6%	$Chi^2 = 1.39$	.49
Treatment Compliance					
Number of drinks/week	–	5.83 (1.30)	5.75 (1.39)	F = 0.13	.72

Standard deviations are in parentheses

measures [27] as well as a more realistic estimate of treatment effects in the real world where people drop out of treatment [28].

In compliance with CONSORT guidelines [15], the analytic plan focused on documenting group × time interactions. Intervention group and group × time interaction terms were entered as fixed effects, with outcome measures modelled using maximum likelihood estimation with a first-order autoregressive covariance structure and with homogeneous variances to account for the correlation between time-points. High-low psychopathy groups were based on a median split of total APSD scores to test for the moderating effect of psychopathic-like behavior on group × time interactions and illustrate findings. This moderation was additionally tested using a dimensional measure of ASPD to assess robustness. Analyses focused on change from baseline within each group as per our prior RCTs [6, 17], with the primary outcome based on one overarching parent-report and one child-report measure of antisocial behavior (see below). False discovery rate control [29] was employed to control for Type I error. Effect sizes are Cohen's d [30], with positive effect sizes indicating improvement relative to baseline. All confidence intervals reports are 95%. Chi-square analyses were conducted on blinding data (perceived group versus actual group). Figures are baseline corrected to illustrate effects. All tests are two-tailed. All analyses were conducted using SPSS (version 23).

To provide overarching constructs of antisocial behavior, factor analysis was conducted on the 7 self-report and 7 parent-report sub-scales of antisocial behavior (see online Supplement for full analytic details).

Results

Participant flow, recruitment, and attrition

Full details on participant flow, including enrollment, group allocation, and follow-up are given in Fig. 1. No participant loss was observed on baseline assessment after randomization. Of the 324 participants, 26 (8.0%) were lost to follow-up at either 6 or 12 months (13 from omega-3, 10 from

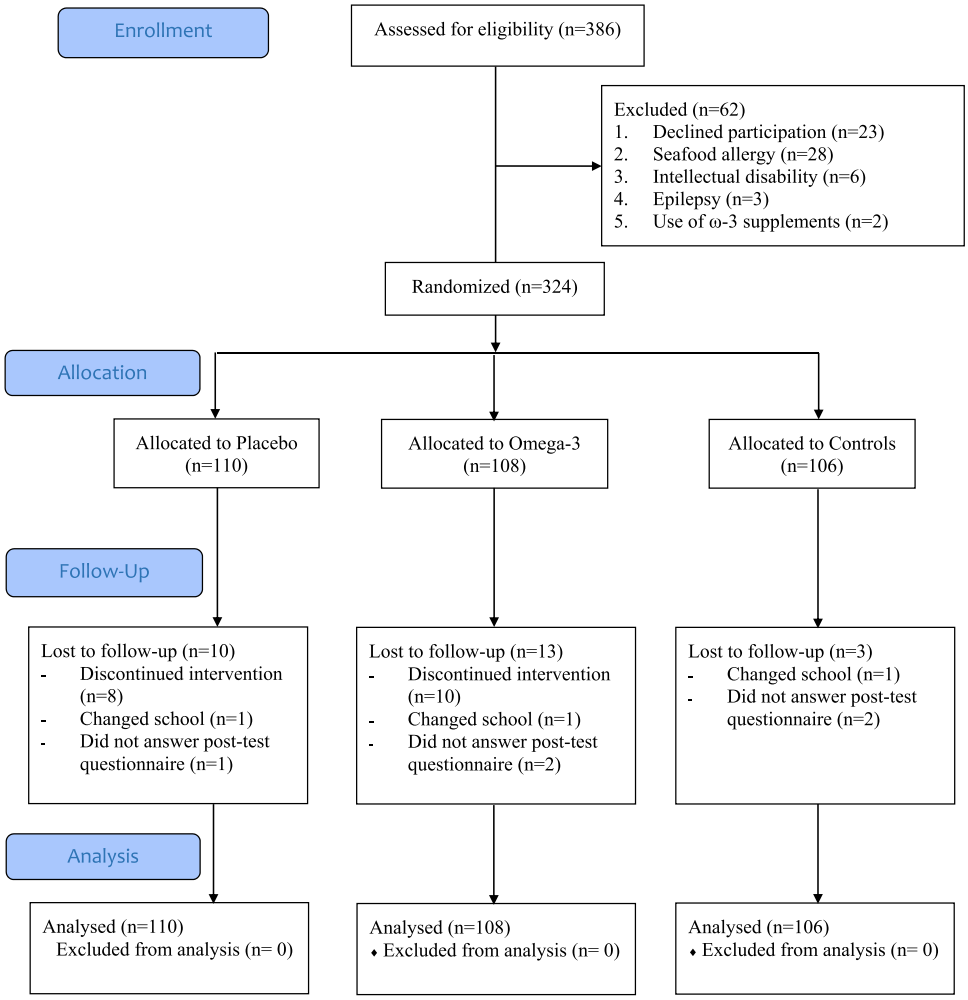

Fig. 1 CONSORT diagram giving details of subject flow on enrollment, group allocation, follow-up, and data analyses

placebo, 3 from controls—see Fig. 1 for detailed reasons for loss). Groups did not significantly differ in this attrition (chi-square = 1.96, df = 2, $p = 0.38$).

Demographics and adherence to protocol

Demographics

Demographic data are reported in Table 1. No significant group differences were observed on age, sex, income, housing, parental education, baseline self-report antisocial behavior, and baseline parent-report antisocial behavior, documenting that randomization and stratification procedures were successful. Further details on parent and child assessment measures are given in the online Supplement.

Adherence to protocol

The mean number of drinks consumed per week by the placebo and omega-3 groups are provided in Table 1. There was no significant group difference in compliance rates, documenting equal adherence to the protocol ($p = 0.72$).

Blinding success

Groups did not differ in their guess on which of the two drink groups they had been allocated to ($p = 0.49$), with 76.0% of the placebo group believing they were assigned to the omega-3 group, compared to 72.6% in the omega-3 group. This indicates that the blinding was successful.

Adverse events

No negative side effects were reported by either child or parent. Only two children reported a minor negative reaction (stomach ache), in both cases from the placebo group. One parent reported a minor adverse event (unpleasant taste) on behalf of the child, in this case from the omega-3 group. No participant withdrew due to these minor events.

Factor analyses of parent and child reports of antisocial behavior

Full details on factor analyses are provided in the online supplementary materials. Briefly, child reports of the seven antisocial behavior scales and parent reports of the same seven antisocial behavior scales were factor analyzed separately in order to provide overarching constructs of antisocial behavior, to aid in reducing Type I error, and to produce more reliable indicators of antisocial behavior than could be obtained from single indicators. Findings provided support for one factor of child self-report antisocial behavior and one parent factor and for the robustness of the factor structure over time and across informants, with the proviso that in both cases the callous-unemotional scale did not load on these factors and was dropped from analyses.

Child reports on treatment effects

Unadjusted means from mixed effects analyses for child-reported and parent-reported measures at all three time points are detailed in Table 2. Analyses below are based on the estimated marginal means. All findings below survived false discovery rate control.

The treatment group x time interaction was non-significant, $F(4,576) = 1.15$, $p = 0.33$.

The treatment group x time x sex interaction was significant, $F(9,445) = 2.30$, $p = 0.016$. Results are illustrated in Fig. 2. While no omega-3 effect was observed in males, females in the omega-3 group showed a significant reduction in antisocial behavior 6 months post-treatment compared to baseline (mean difference = 0.373, CI 0.016 to 0.730, $p = 0.041$, $d = 0.35$, CI 0.05 to 0.63), whereas the females in the two control groups showed no change in time. No other comparisons were significant.

The treatment group × time × psychopathy group was significant, $F(8,552) = 3.47$, $p = 0.012$. This 3-way interaction was also confirmed when utilizing a continuous psychopathy moderator variable ($p = 0.006$). To illustrate the interaction, antisocial scores for all three treatment groups for the high and low psychopathy groups are depicted in Fig. 3. For the omega-3 group only, antisocial behavior was significantly reduced compared to baseline at 6 months ($p = 0.039$, mean difference 1.01, CI = 0.05 to 1.96, $d = 0.19$, CI 0.03 to 0.41) only in the high psychopathy group. No other comparisons were significant.

Table 2 Means with 95% confidence intervals (in parentheses) from mixed effects models on child behavior outcomes in omega-3 ($n = 108$), placebo ($n = 110$) and control ($n = 106$) groups for the three assessment periods for both child and parent reports

Group	Time	Child report antisocial	Parent report antisocial
Controls	0 months	.10 (− .09, .29)	.15 (− .05, .35)
	6 months	.11 (− .08, .30)	.15 (− .06, .36)
	12 months	.01 (− .19, .20)	.07 (− .14, .29)
Placebo	0 months	− .06 (− .25, .14)	.05 (− .15, .25)
	6 months	.03 (− .17, .23)	− .11 (− .32, .10)
	12 months	.03 (− .17, .22)	− .04 (− .25, .17)
Omega-3	0 months	− .02 (− .22, .18)	− .16 (− .36, .04)
	6 months	− .15 (− .35, .05)	− .08 (− .30, .14)
	12 months	− .03 (− .23, .17)	.04 (− .17, .26)

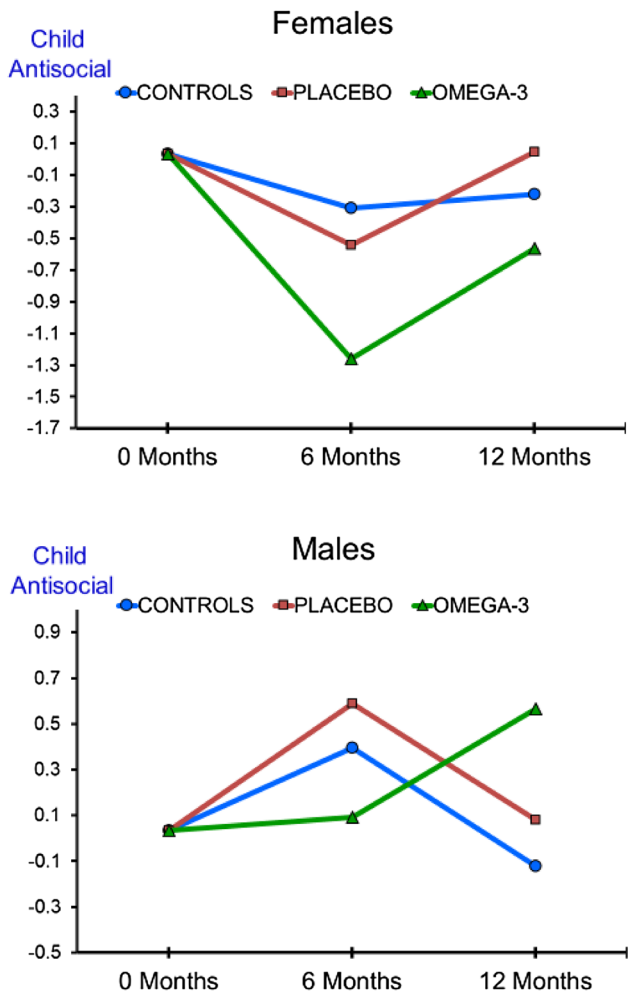

Fig. 2 Illustration of the group × time × sex interaction ($p = .016$). For females (upper figure), only the omega-3 group shows a significant decline in antisocial behavior from baseline to 6 months ($p < .041$). No significant treatment group differences were observed in the males (lower figure)

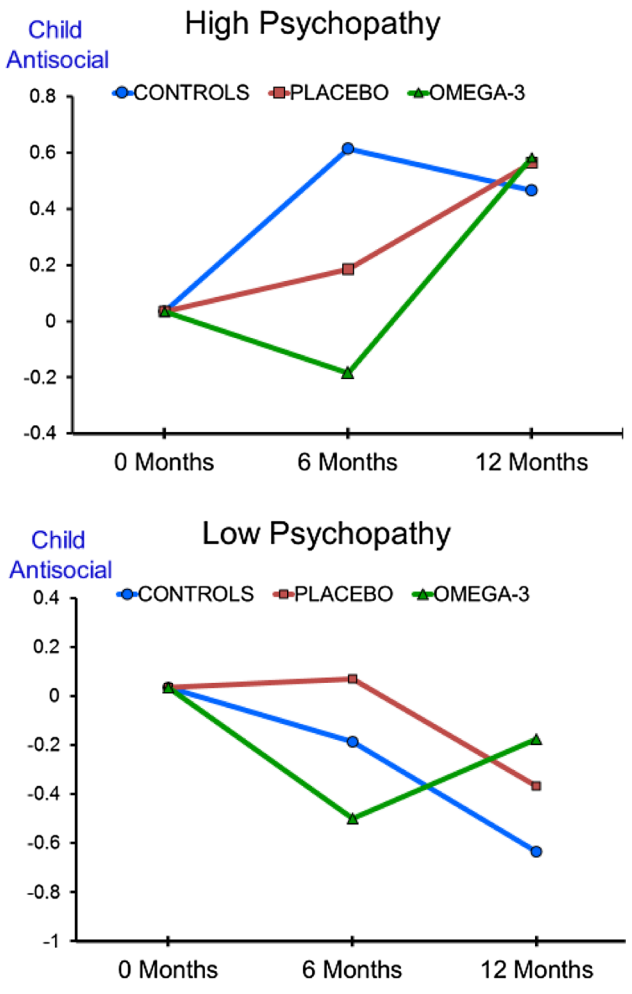

Fig. 3 Illustration of the group × time × psychopathy group interaction ($p = .006$). For the high psychopathy group (upper figure), only the omega-3 group shows a significant decline in antisocial behavior from baseline to 6 months ($p < .039$). No significant treatment group differences were observed in the low psychopathy group (lower figure)

Parent reports on treatment effects

The treatment group × time interaction was non-significant, $F(4,393) = 1.31$, $p = 0.27$, as were other interactions ($p > 0.21$).

Discussion

This study assessed the efficacy of omega-3 supplementation in reducing antisocial behavior in an East Asian population, and evaluated whether gender and psychopathic-like traits moderated treatment outcome. Support for the overall treatment effects was mixed, with significant short-term improvement being found for females ($d = 0.35$), but not for males. Psychopathic-like traits moderated treatment outcome ($p = 0.006$) with omega-3 supplementation reducing self-report antisocial behavior in children with high levels of psychopathic-like traits by the end of treatment ($d = 0.19$). Findings are the first to document efficacy of omega-3 in reducing antisocial behaviors in children with psychopathic-like traits. While effects were found only for child reports, findings nevertheless provide a new vista for treatment of psychopathic-like children and adolescents which could be explored further in future studies.

The efficacy of omega-3 supplementation in reducing antisocial behavior in children with psychopathic-like traits raises the question of how and why such supplementation could result in positive outcomes. A lacuna in our knowledge is that no prior study has taken a biological approach to treating psychopathic-like traits in children. With some exceptions [31], biological interventions for antisocial

behavior in past reviews of treatment studies are conspicuous by their complete absence [10, 12, 13]. This is more surprising in that there is reason to believe that there may be a particularly stronger biological basis to antisocial behavior in psychopathic-like children compared to non-psychopathic children. For example, a notable finding is the much stronger heritability for antisocial behavior in children with high psychopathic-like traits (81%) compared to children with more normative levels of these traits (30%) [32]. A review of 32 studies investigating biological correlates of child psychopathic-like behavior has highlighted the influence of these markers in antisocial children with psychopathic-like traits, compared to antisocial non-psychopathic children for whom inadequate socialization experiences are argued to play a stronger role [12]. Yet another comprehensive review of neurobiological risk factors for psychopathic-like behavior affirms the importance of biological influences for these children, while recognizing the role of social / psychological influences [13]. If it is the case that there is a stronger neurobiological basis to antisocial behavior in more psychopathic-like children compared to those low in psychopathic-like traits, it could be hypothesized that biological interventions like omega-3 which target brain structure and function [33] could be more likely to especially benefit psychopathic-like children.

The primary hypothesis of this study, that omega-3 should reduce overall antisocial behavior, was supported for females but was not observed for males. These more mixed findings lie in contrast to prior omega-3 RCTs which have, taken together, shown somewhat stronger efficacy in reducing antisocial behavior in other countries [5, 34, 35]. In this context one cross-cultural difference should be considered. This study was conducted on school-children in Hong Kong. Hong Kong has the second-highest level of marine fish per capita in the world [36]. It is possible therefore that the failure for omega-3 supplementation to have an across-the-board effect in reducing antisocial behavior could be a function of the relatively high intake of fish (and hence omega-3) in this region. Cross-national research has documented a relatively strong negative correlation ($r = -0.68$) between sea-food consumption throughout the world and homicide rates [4], and conceivably in Hong Kong there may be a ceiling effect that limits the impact of omega-3 in enhancing neurobiological functioning and reducing antisocial behavior. Despite the non-significant results, the direction of effects observed indicate that the omega-3 group tended towards a small *reduction* in child-report antisocial behavior at 3 months ($d = 0.13$) in comparison to small *increases* in both controls ($d = -0.01$) and placebo ($d = -0.08$) groups. This group difference in effect sizes is not too dissimilar from the overall effect size of $d = 0.20$ reported in one meta-analysis [7]. Future research could test whether effect sizes in treatment studies are somewhat larger in countries with less fish intake than in Hong Kong and are stronger for females.

While significant effects were obtained for child self-reports, results for parent-reports were non-significant. Low correspondence between multiple informant ratings has been argued to be the rule rather than the exception in child psychopathology research [37]. The current study was no exception, with child-reports and parent reports sharing less than 7% of the variance ($r = 0.26$). Furthermore, controlled trials often reveal discrepancies across raters [38]. Although many researchers treat informant discrepancies as measurement error [39], parent and child reports could both reflect valid indicators of antisocial behaviors perpetrated in different situational contexts. While we did not a priori design this study to test between these competing perspectives, some limited data bear on the issue of reliability and validity of parent and child reports at baseline. Reliability analyses for the six parent-report scales resulted in a Cronbach's alpha of 0.85 which is very comparable to the six self-report measures (alpha = 0.83). With regard to validity, however, self-reports of antisocial behavior were associated in the expected direction with low level of mothers' education ($d = 0.24$, $p = 0.03$) and (male) gender ($d = 0.30$, $p = 0.007$), while parent-reports were not significantly associated with these variables ($p > 0.31$). While we cannot definitely conclude from these limited post-hoc data that significant findings were found for self-report but not parent-report because the latter are less valid, future studies could be designed to a priori assess whether multi-informant discrepancy represents error or alternatively whether meaningful differences between raters exist [39].

To what extent can the current findings be regarded as clinically significant? It should be clarified at the outset that this is a community sample as opposed to a clinical sample. Bearing in mind this caveat, the finding of reduced antisocial behavior in females taking omega-3 with an effect size of $d = 0.35$ is not large and lies in the small to medium range [30]. Similarly, the effect size for reduced antisocial behavior in high-scoring psychopathic-like individuals was small ($d = 0.19$).Others have argued, however, that the threshold for clinical significance should be less stringent for treatments which are relatively low-cost, less invasive, and protect against a serious issue [40]. Given that nutritional supplementation is relatively non-invasive, has a modest cost, and could protect against serious violence, it is suggested that the current modest effects sizes cannot be dismissed as of no practical utility. This is particularly true of those presenting with psychopathic-like behavior given the conclusions from some reviews that treatment efficacy for antisocial behavior in such individuals is minimal or non-existent [10, 11]. Because no prior studies have examined omega-3 efficacy in psychopathic-like individuals, we conclude that

these findings in particular may be of some clinical significance, pending replication.

Limitations of this study need to be recognized. First, because the placebo drink contained vitamins and antioxidants, this could have psychoactive properties, contributing to the slight declines (albeit non-significant) in females and in the low psychopathy group taking the placebo drink. Second, while we stratified on age and sex, we did not stratify on outcome measures. While such stratification would have helped to ensure balanced representation across the three groups on the outcome measures, there were no significant group difference on the outcome measures at baseline. Third, given the inherent variability in results of individual studies, careful replication and extension of the current findings from methodologically sound RCTs is required.

In conclusion, this study builds on a growing body of evidence from the nascent field of nutritional psychiatry to suggest that omega-3 supplementation could play some role, albeit at a modest level, in ameliorating antisocial behavior in children with psychopathic-like behavior, a group who have been strikingly resistant to change based on tradition psychological interventions [10]. Given the increasing evidence that persistent antisocial behavior is neurodevelopmental in nature [41, 42], intervention approaches need to increasingly recognize the biological contribution to antisocial causation and how benign biological interventions may have utility.

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Compliance with ethical standards

Conflicts of interest None.

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