Author’s response to reviews

Title: Association between anxiety and aggression in adolescents: a cross-sectional study

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Responses to reviewers’ comments

Reviewer reports:

A. Bilgic (Reviewer 1): This is, in summary, an interesting paper examining the relationship between severity of anxiety and aggressive behavior in a sample of 2432 adolescents. The authors reported that higher anxiety scores are independently related with higher aggression scores and these relationships are more stronger for anger and hostility then physical and verbal aggression. The authors may find as follows my main comments/suggestions.

1. The introduction is insufficient. Previous studies regarding this issue should be discussed in more detail. I suggest to cite and discuss the paper which has been published on Aggressive Behavior in 2017 (PMID: 28217970), Development and Psychopathology in 2016 (PMID: 27739391), Child Psychiatry and Human Development in 2017 (PMID: 27033363), Aggressive Behavior in 2014 (PMID: 23868672) etc.

--> Your suggestions were included and extensively dealt with in the Introduction as follows: Several studies have reported the link between anxiety and aggression in childhood. It was
revealed that reactively aggressive children at age six were significantly more anxious than their non-aggressive counterparts [8]. Also, in elementary school students, relational and physical aggression were suggested as the strongest predictors of anxiety [9]; in addition, a study on American 2nd, 3rd, and 4th graders demonstrated a relationship between baseline anxiety symptoms and higher levels of relational aggression over a 1-year period [10]. Furthermore, a study including children with attention-deficit/hyperactivity disorder reported that disruptive behavioral disorders were associated with reactive–proactive aggression and anxiety sensitivity [11].

2. The introduction should be strengthened by providing a more explicit presentation of the knowledge gaps in the field and how this study addresses some or all those gaps. The general background and underlying hypothesis for studying this variable in this sample seems a bit poorly developed.

--> The background information was adequately modified and reinforced as follows: Depression and anxiety are the strongest predictors of suicidal ideation, threats, and plans [18]. The increase in internalizing distress throughout adolescence is particularly concerning given that suicide has been the leading cause of death among Korean youths aged 15-19 [19]. Thus, developing a more in-depth understanding of the relationship between anxiety and aggression throughout adolescence is of paramount importance. Despite this significance, few studies have linked anxiety and aggression in adolescents.

3. We can not use ambiguous expressions in the Results section. In page 6, line 36, the statement "there were more than twice as many girls than boys" should be removed and rewritten more clearly.

--> The expression is rewritten as suggested: “…. RCMAS and 69.9% of them were girls.”

4. The authors primarily should discuss main findings of the study. Girl-to-boy prevalence ratio of anxiety is not a main issue for this study. I think the second paragraph of discussion section should be related to the link between anxiety and aggression.

--> The discussion has been reorganized based on the importance of main findings. Specifically, the second paragraph has been moved to the fifth.

5. Similar to the introduction, the discussion section is also insufficient. Previous studies regarding this issue should be discussed in more detail.
More details of previous studies were added in the Discussion section: Adolescence is a period in which aggressive behavior tends to increase. Accordingly, it is essential to understand how the specific subtypes of aggression during adolescence contributes to anxiety increase, or vice versa. Previously, it was shown that aggression was a risk factor for the development of internalizing problems (depression and anxiety) in male adolescents. Although significant results were reported in that study, the relatively low internal consistencies associated with the anxiety measure likely weakened the reported results [25].

6. The manuscript needs to be reviewed for the quality of language by a native English speaker.

Annabeth Groenman (Reviewer 2): This paper looks at the relation between anxiety and aggression in a large group of Korean adolescents. Overall this paper looks at an interesting question and the dataset is an impressive size. Generally speaking, this paper has promise, but the execution is bit messy.

Major points:

1. the statistical analyses are not well described and, from what I do understand, are not the best for the number of measures looked at. Groups were made based on the questionnaire data. It is very clear how the groups were made, I would suggest describing the exact way in which this was done. The same stands for the aggression questionnaire. Furthermore, a manova was done in the first step, but in the result is seems like many anova's were done. A backwards approach to model building is described, but I do not seem the point in using ANOVAs first and later finding out that all those tests were not necessary because variation of one variable was explained by another variable. I would suggest asking someone with more statistical knowledge about possibilities for more up to date model building. I could suggest looking into more sophisticated methods like LASSO, that take out the researchers' degrees of freedom. Otherwise, please put some care into describing the analyses that were performed.

We performed multivariate analysis of variance (MANOVA) for Table 2. In Table 2, there were five response variables (total and subdomain scores of Aggression Questionnaire). Because using multiple ANOVAs inflates type 1 error rates, MANOVA is used to help control for the inflation.
Table 1 and Table 2 showed the factors associated with anxiety proneness and aggression propensity, respectively, and Figure 1 showed the relationship between anxiety proneness and aggressive behaviors. After univariable analyses, multivariable logistic regression analysis with backward selection was used to identify independent prognostic factors for anxiety proneness (Table 3), and the association between anxiety proneness and aggression behavior remained significant after controlling other variables.

Accordingly, we revised the statistical analysis for clarification since there were some confusing sentences, and final statements are as follows: The independent t-test was used to compare continuous variables between participants with and without anxiety or aggression propensity. The chi-square test was used for categorical variables, and data were expressed as percentages. A multivariate analysis of variance (MANOVA) was conducted to examine differences in the subdomains of aggression propensity (physical aggression, verbal aggression, anger, hostility, and total), since each of the subdomains of aggression was correlated with at least one other subdomain. To analyze the relationship between anxiety and aggression propensity, Pearson’s correlation coefficient was used. The area under the receiver operator characteristics (AUROC) curve was calculated for the cut-off of aggression scores. Multivariable logistic regression analysis was performed, using the backward stepwise method. The anxiety and control groups were classified according to the RCMAS (control group: RCMAS ≤25, anxiety group: RCMAS >25). Odds ratio (OR) and adjusted OR (AOR) were calculated with 95% confidence interval (CI). The model fit of the prediction model was assessed by an analysis of the AUROC. P value of less than 0.05 was considered statistically significant. Statistical analysis was conducted using SPSS Statistics for Windows 20.0 (IBM Cop., Armonk, NY).

In addition, we additionally performed LASSO logistic regression using the R package glmnet, as commented. Candidate prognostic factors including aggression scales (total aggression score for Model III, and higher aggression score group [≥ 69] for Model IV, respectively) were initially included in the variable selection procedure, and eight factors were selected for Model III and 12 for Model IV. All factors included in Model I and Model II (in submitted text) were selected in Model III and Model IV and showed similar trends. Indigestion was additionally included in Model III compared to Model I, and muscle pain, indigestion, heartburn, and sleeping pills were added in Model IV compared to Model II. Although LASSO logistic regression selected more variables than backward selection, both methods attained roughly the same accuracies (91.9% and 91.7% for Model I and II vs 91.8% and 91.5% for Model III and IV), as well as AUC values (0.853 and 0.827 for Model I and II vs 0.853 vs 0.830 for Model III and IV). As the simplest model, if not worse, is most likely to be the best (typically referred to as “Principle of Parsimony” or “Occam’s Razor”), Model I and Model II were finally chosen.

2. The measures concerning anxiety and aggression are well described, but a lot of information about the other measures is missing. For example, on page 5 line 44-46 it states:
"headache, muscle pain, constipation and asthma, and medication history of consuming painkillers, digestives and sleeping pills within 30 days." But in the Table 1 we find out that other measures (e.g. caffeine use, alcohol use, smoking, muscle pain, scoliosis) were taken. Information should be concise.

--> We’ve inserted the measures mentioned in the table but missing in the Method section as follows: Demographic information included age, gender, caffeine intake, alcohol consumption, smoking, history of medical symptoms such as headache, muscle pain, scoliosis, constipation, dyspepsia, heartburn, atopic dermatitis, sinusitis, and asthma, and medication history of consuming painkillers, digestants, and sleeping pills within 30 days.

3. The language use is bit awkward and I would suggest some attention is paid to this.

--> The manuscript was reviewed and extensively revised by a native English speaker.

4. The combination of aggression (on which the main conclusions are) and medical conditions in relation to anxiety are difficult to glue together for me. I do not see how these would complement each other, and why they are described in one paper.

--> We have included other medical conditions or medications in order to investigate what other factors are related to anxiety and aggression and also to rule out any possible effects as confounding variables.

Minor points:

1. Page 3, line 7/8 suggest that anger and aggression are the same thing. Also, a paragraph should be more than 2 sentences.

--> The first paragraph has been changed as follows: Adolescence is a critical developmental period by which social, emotional, and physical changes to the body can build up negative self-perceptions [1] Previous studies have shown that adolescent behavior is highly determined by emotions [2,3], whereas aggression in adolescent males was a risk factor for the development of internalizing problems such as anxiety and depression [4]. In addition, there is growing concern for the co-occurrence of behavioral, emotional and cognitive problems.

2. Page 3 line 29/30: friendships are social relationships.

--> “… or friendships” is deleted.
3. Page 4 line 4. A dot is missing after kim et al.

--> A dot is added after Kim et al.

4. Page 4 line 10-15. The link between stress and anxiety should be described

--> The following was added as commented: Adolescent stress has been linked to negative mental health outcomes such as anxiety and depression [14].

5. Page 4 study population: Please describe the population a bit better. How many people were approached, how many people included, did participants gave consent, ethical considerations (declaration of Helsinki?), males, females, school levels etc.

--> The following sentences were added in the Method: A total of 2,432 students participated in the survey, and 1,933 individuals completed the questionnaire, showing a response rate of 79.5%. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

--> The following sentences were included under Declaration section at the end of the manuscript: This study was approved by the Honam University Review Board (Approval No. 1041223–201510– HR-090-01). Informed consents were obtained from students’ parents.

--> Characteristics of survey participants were described at the beginning of Results: The mean age was 15.0 ± 1.9 years and 897 (47.1%) were boys. The distribution of the students across the schools was as follows: 930 students (48.1%) in middle school, 1,001 (51.8%) in high school, and 2 (0.1%) unspecified. Among them, a total of 163 (8.4%) adolescents were classified as anxiety group based on RCMAS, and 69.9% of them were girls.

6. Page 5 line 13/14: the reference to the Korean measure is missing

--> Reference no. 21 was inserted after “… and Richmond.”

7. Page 5 line 31: the reference to the Korean measure is missing

--> Reference no.22 was inserted after “… participants.”
8. Page 5 line 46: what are digestives? I only know them as cookies.

--> Digestants is used instead of digestives.

9. Page 6 line 6. AUC is the more commonly used abbreviation

--> Although AUC is also used, we felt that it is prudent to eliminate any ambiguities, if possible. For example, AUC is used for a totally different parameter in the field of pharmacokinetics.

10. Please check the rest of the manuscript for these types of errors.

--> We checked and revised the manuscript as your recommendation.

11. Please rewrite the first paragraph of the discussion. Now it is just a mere summary of the results.

--> The first paragraph of the discussion was rewritten as commented: This study presents a clear and specific association between anxiety and aggression in Korean adolescents. In particular, among the subdomains of aggression, anger and hostility were more closely associated with anxiety than physical and verbal aggression; this indicates an interesting relationship between indirect aggression and anxiety.

12. I would focus the discussion on the main results and not on the AUC results of the AQ.

--> To focus on the main results, we deleted a statement on the AUROC, as suggested.

13. Why are there so few people in the aggression propensity scores described in the second table?

--> The numbers in Table 2 describe the scores of aggressive propensity, not the number of students. For example, the ‘45’ under ‘Physical’ in Table 2 indicates a score of 45, not the number of students that show physical aggression.