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Testosterone and cortisol modulate the effects of empathy on aggression in children

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ABSTRACT

This study aimed to analyze the potential moderating role of circulating testosterone, cortisol and estradiol levels on the attenuating effect of empathy on aggression in children. Participants were 139 children (80 boys and 59 girls) from the 3rd year of primary school (age 8). Their aggressive behavior was measured by the Direct and Indirect Aggression Scale, an instrument which uses peer rating; empathy was measured using the Empathy Quotient-Child Version. Hormone levels (testosterone, cortisol and estradiol) were analyzed using an enzymoimmunoassay technique in saliva samples. A regression analysis revealed an interaction effect of *empathy x testosterone* in girls, with higher levels of empathy corresponding to lower levels of aggression at both moderate and low testosterone levels. In boys, an interaction effect of *empathy x cortisol* was observed, with lower levels of empathy corresponding to higher aggression levels at moderate and high cortisol levels, and higher levels of empathy corresponding to lower aggression levels again at moderate and high cortisol levels. Our results indicate the importance of taking the interaction of psychological and biological factors into account in order to gain greater insight into the complex mechanisms underlying aggressive behavior.

1. Introduction

The search for markers of aggression during childhood is a particularly relevant area of research, since the results of intervention and prevention during this developmental stage are more promising than those obtained during later stages (Tremblay, 2008; Tremblay et al., 2018). Although many individual variables (both psychological and biological) have been analyzed in relation to aggression in children (Tremblay et al., 2018), the psychobiological approach to this question is of particular importance, as it analyzes the joint, interactive influence of both psychological and biological variables. This is especially relevant in those cases in which an association of some kind has been established independently between both types of factors and aggressive behavior, or where a direct relation has been observed between the psychological and biological factors in question- as is the case with empathy and hormones such as testosterone, cortisol and estradiol. Many studies have established a relation between empathy measures and aggression levels (Berger et al., 2015; Euler et al., 2017; Garaigordobil and García, 2006). Also, although they are scarcer, other works have observed an association between testosterone, cortisol and estradiol levels and aggressive behavior in children (Azurmendi et al., 2016; Barzman et al., 2013; Sánchez-Martín et al., 2000, 2011). Furthermore, an association has been observed between the aforementioned hormones and empathy (Moul et al., 2018; Pascual-Sagastizabal et al., 2013). Thus, given the associations described above between hormones-aggression, empathy-aggression and hormones-empathy, it is reasonable to assume the possibility of interaction effects between hormones and empathy on aggressive behavior in children. However, to the best of our knowledge, no study to date has analyzed the moderating role played by testosterone, cortisol and estradiol levels in relation to the attenuating effect of empathy on aggressive behavior in children. The present study aims to fill this gap.

In relation to testosterone, a large body of evidence points to a positive relation between this hormone and aggression, in both humans and other animal species (Archer, 2006; Trainor et al., 2009)- although studies on humans have mainly been carried out with pubescent or

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post-pubescent individuals, with only a few studies focusing on pre-pubescent stages. Of these, some have reported a positive correlation between testosterone and other androgens and aggressive behavior (Azurmendi et al., 2006; Barzman et al., 2013; Sánchez-Martín et al., 2000), particularly in boys, whereas others have failed to find any association between baseline testosterone levels and aggressive behavior (Popma et al., 2007).

In general, low cortisol levels have been associated with more aggressive behavior in children and adolescents (McBurnett et al., 2000; Virkkunen et al., 2004), and has even been suggested that low cortisol levels during childhood may be considered a risk factor for the development of aggressive behavior later in life (Moya and Ramirez, 2010). Nevertheless, some studies have found a positive relationship between cortisol and aggressive behavior (Azurmendi et al., 2016; Böhnke et al., 2010; Feinberg et al., 2011; Lopez-Duran et al., 2009), and despite the large body of research that supports the idea of some kind of relationship between cortisol levels and aggression, some authors have failed to find any such association (Golubchik et al., 2009).

Very little research has been carried out into the possible association between estradiol levels and aggression, and the results of the few studies that have been conducted are inconclusive. Whereas some authors have reported a positive association between estradiol levels and aggression in both boys and girls (Finkelstein et al., 1997), others found said positive correlation only in girls (Inoff-Germain et al., 1988). Furthermore, Gladue (1991) found a negative correlation between estradiol and aggression in women, and a positive one in men. In a longitudinal study with children, Azurmendi et al. (2016) observed that boys whose aggressive behavior increased most from age 8 to age 10 were also those whose estradiol levels decreased most notably.

One individual variable to which a great deal of attention has been paid in the study of aggressive behavior is empathy. Empathy is generally defined as the ability to comprehend and share another's emotional state (Hoffman, 2000) and is understood as a multidimensional construct which contains both cognitive and affective aspects.

Empathy is considered a strong inhibitor of aggressive behavior (Campbell, 2006).There is general agreement among authors that higher levels of empathy are associated with reduced aggression levels and an increase in prosocial behavior (Jolliffe and Farrington, 2006; Warden and Mackinnon, 2003).

In light of the above, the aim of the present study was to analyze the influence of empathy, hormones and hormone x empathy interactions (testosterone x empathy, cortisol x empathy and estradiol x empathy) on aggressive behavior in boys and girls. Given that the majority of studies with children (in some cases very scarce to begin with, such as is the case with estradiol) suggest positive testosterone-aggression, cortisol-aggression, and a negative estradiol-aggression associations and empathy-aggression association, we expected to find that: a) children with high testosterone levels and low empathy levels would score higher for aggression; b) children with high cortisol levels and low empathy levels would score higher for aggression; and c) children with low estradiol levels and low empathy levels would score higher for aggression. Given that sex differences have been found previously in relation to a number of the variables analyzed in the study, and even some of the associations between them, special attention was paid here to this aspect. In other words, when searching for the psychobiological markers of aggressive behavior in early childhood, it is important to consider the possibility that some of these markers may be specific to boys, and others may be specific to girls. The present study aims to help identify the psychobiological mechanisms which underlie aggressive behavior in boys and girls, exploring the way in which hormones and psychological variables interact to influence said behavior, in line with other studies which have found similar interactions (Sánchez-Martín et al., 2011; Pascual-Sagastizabal et al., 2013).

2. Methods

2.1. Participants

The sample group comprised 139 subjects, 80 boys and 59 girls, in their 3rd year of primary school (all were 8 years of age), drawn from four schools in the study area (Northern Spain). To select the sample, several schools were chosen in the province where the researchers' university is located, with priority being given to schools with more than one class for the selected age group. The families of the 139 children gave their written consent for their sons and daughters to participate in the study. None of the tests used were invasive and they were all administered by qualified members of the research team at 09.00 h in the classrooms, adapting to the school calendar. The project was approved by the Ethics Committee of the institution to which the authors belong; the procedure followed also complied with all pertinent national legislation.

2.2. Aggressive behavior measure

Aggressive behavior was assessed using the Spanish language version of the DIAS (Direct and Indirect Aggression Scale) (Björkqvist and Österman, 1998). Several studies have verified this peer estimation scale as an adequate instrument for measuring different types of aggression in children and adolescents (Björkqvist et al., 2001; Valles and Knutson, 2008). Aggressive behavior is measured through 24 items (for example: Does he/she hit a lot? Does he/she shut others out of the group?), regarding which children evaluate the behavior of only their same-sex classmates on a five-point Likert-type scale ("never", "seldom", "sometimes", "quite often", "very often"). Items refer to physical aggression, verbal aggression and indirect aggression. Bearing in mind the close correlation which exists between these subscales ($r \geq 0.97$), a global aggression score was calculated for each child based on the scores obtained on all three. The reliability coefficient for this questionnaire in our sample was $\alpha = 0.97$.

As stated above, peer estimation was carried out in accordance with sex (i.e. children were only asked to evaluate their same-sex classmates). This decision was due to the social segregation typical of this age group, in which play and friendship groups are generally sex segregated, with the majority of boys socializing and playing with other boys, and the majority of girls socializing and playing with other girls. Thus, asking children questions about the opposite sex may give rise to estimation errors due to prejudice or lack of knowledge.

2.3. Empathy measure

Empathy was measured using the Empathy Quotient-Child Version (EQ-C), i.e. the child's version (Chapman et al., 2006) of the instrument developed by Baron-Cohen and Wheelwright (2004) for adults. In the EQ version for adults it has been suggested that there may be three factors that allude to the characteristics cognitive, emotional and social skills (Lawrence et al., 2004) but in the child version, the EQ-C yields an overall empathy score (Auyeung et al., 2009).

In this test, parents evaluate their children's capacity for empathy. It comprises 27 items rated on a four-point Likert-type scale ("definitely agree", "slightly agree", "slightly disagree" and "definitely disagree") (for example: "My child likes to look after other people"; "My child would worry about how another child would feel if they weren't invited to a party"). The reliability obtained in our sample was $\alpha = 0.78$.

2.4. Hormone level measures

To analyze baseline hormone levels (testosterone, cortisol and estradiol), two saliva samples were collected by the passive drool method in hygienic collection kits within a six-week time frame. Prior to the sample collection, children received no instructions to refrain from

consuming food or drink. Samples were collected in the classrooms on weekdays at 09.00 h, before lessons started, in order to avoid concentration changes due to diurnal hormonal fluctuations. To help them salivate, the children were offered a sweet on the condition that they were not allowed to eat it until they had given a large enough sample. Samples were processed in the laboratory and stored at -80 °C until analysis. They were assayed in duplicate for each subject using an ELISA (Enzyme-Linked Immunosorbent Assay) (Salimetrics, State College, PA, USA). For hormone levels, the average intra-assay coefficient of variation (CV) was less than 3% and the inter-assay coefficient of variation (CV) was less than 14%, calculated on the basis of control samples.

In order to establish a baseline for each child's hormonal levels, Pearson correlations were performed to explore the relationship between the hormonal levels of the two saliva samples collected. Due to the positive correlations observed for all three hormones (testosterone $r = .597$, $p < .001$, cortisol $r = .560$, $p < .001$, estradiol $r = .251$, $p = .008$), the two values were averaged to obtain a measure for each hormone and subject. These values were the ones used for the statistical analyses.

2.5. Statistical analysis

Before carrying out the statistical analyses, all study variables were transformed into Z-scores in order to eliminate range disparity. Once it had been established that the variables did not follow a normal distribution, we managed to normalize them using the Blom transformation offered as part of the SPSS 21.0 statistical package, which is one of the best transformations for dealing with asymmetric distributions (Rodriguez and Ruiz, 2008). The variables were normalized to mitigate the violation of the normality assumption, so as to enable the subsequent parametric analyses to be carried out.

First of all, we conducted an ANOVA to test for sex differences in all the variables. Next, to test for possible associations between the different variables analyzed in the study, we used a sex-based Pearson correlation coefficient. Regression analyses were conducted to study the influence of hormones, empathy and their interactions on aggressive behavior. Since associations and interactions have often been observed between the hormones themselves, it was decided to control for the shared variance between them by including them in the same model, as well as by testing for the potential interaction effect between them on aggressive behavior using an R^2 change analysis. The model obtained from this analysis was established for the entire sample group, and since the sample size did not permit sex differences to be studied through higher-order interactions (3-way interactions), we opted to replicate the model for girls and boys separately. All the variables entered into the regression models were continuous. Finally, we assessed those interactions that were found to be significant, using the moderation analyses described by Hayes (2013) with the Johnson-Neyman technique. All statistical analyses were conducted using the SPSS 21.0 statistical package.

3. Results

3.1. Sex differences, means and standard deviations

Analyses of variance (ANOVAs) were performed to analyze sex differences in all the study variables. The results revealed that girls scored higher in empathy ($F_(1,137) = 14.36$, $p < .001$, $d = 0.66$) than boys. No statistically significant differences were found between boys and girls in any of the other variables (Table 1).

3.2. Correlation analyses

Pearson correlations were conducted separately for boys and girls to study the relationship between aggressive behavior, empathy and hormone levels. As shown in Table 2, aggressive behavior was found to correlate negatively with empathy in both sexes. Moreover, a negative correlation was also observed between estradiol and empathy among boys, and a positive correlation was found between cortisol levels and aggressive behavior among girls.

Table 1
Sex differences, means and standard deviations.

		Boys (n = 80)		Girls (n = 59)		
	Range	Mean	Deviation	Mean	Deviation	F
Aggressive Behavior	0-3	0.64	0.39	0.52	0.35	3.376
Testosterone (pg/mL)	2.44–37.33	14.71	7.62	16.11	7.40	1.186
Cortisol (μg/dL)	0.04–0.79	0.29	0.13	0.29	0.16	.022*
Estradiol (pg/mL)	0.5–7.47	1.92	1.36	1.99	1.10	.098
Empathy	0–54	34.91	7.07	39.12	5.53	14.36***

*** $p < .001$.

Table 2
Correlations between aggressive behavior, empathy and hormonal levels in boys (below, n = 80) and girls (above, n = 59).

	Aggressive Behavior	Empathy	Testosterone	Cortisol	Estradiol
Aggressive Behavior		−.324**	−.015	.074	.076
Empathy	−.328*		.065	.049	.055
Testosterone	.234	−.140		.397**	.476**
Cortisol	.468**	−.177	.542**		.224*
Estradiol	.189	−.377**	.349**	.387**	

** $p < .01$.
* $p < .05$.

3.3. Effects of the interaction between empathy and hormone levels on aggressive behavior

To analyze the effects of empathy, hormone levels and their interactions on aggressive behavior, a regression analysis was carried out for the entire sample, testing two models. The first model included the simple effects of the variables and the interactions between empathy and hormone levels. The second model also included interactions between hormones (*testosterone x cortisol, testosterone x estradiol, cortisol x estradiol*). Since the R^2 change in the second model was not significant ($p = .213$), in accordance with the principle of parsimony, the first model was selected. As shown in Table 3, this model was found to be significant ($R^2 = .22$, $F_(7,131) = 5.278$, $p < .001$) and a statistically significant interaction was observed between cortisol and empathy for explaining aggressive behavior.

Since the sample size did not permit higher-order interactions (with

Table 3
Regression analysis for Aggression.

	Beta	t	Sig.
Empathy	−.346	−4.345	.000***
Testosterone levels	−.001	−0.011	.991
Cortisol levels	.183	2.034	.044*
Estradiol levels	−.133	−1.705	.090
Testosterone*Empathy	.094	0.947	.345
Cortisol*Empathy	−.267	−2.645	.009**
Estradiol*Empathy	−.123	−1.247	.215

*** $p < .001$.
** $p < .01$.
* $p < .05$.

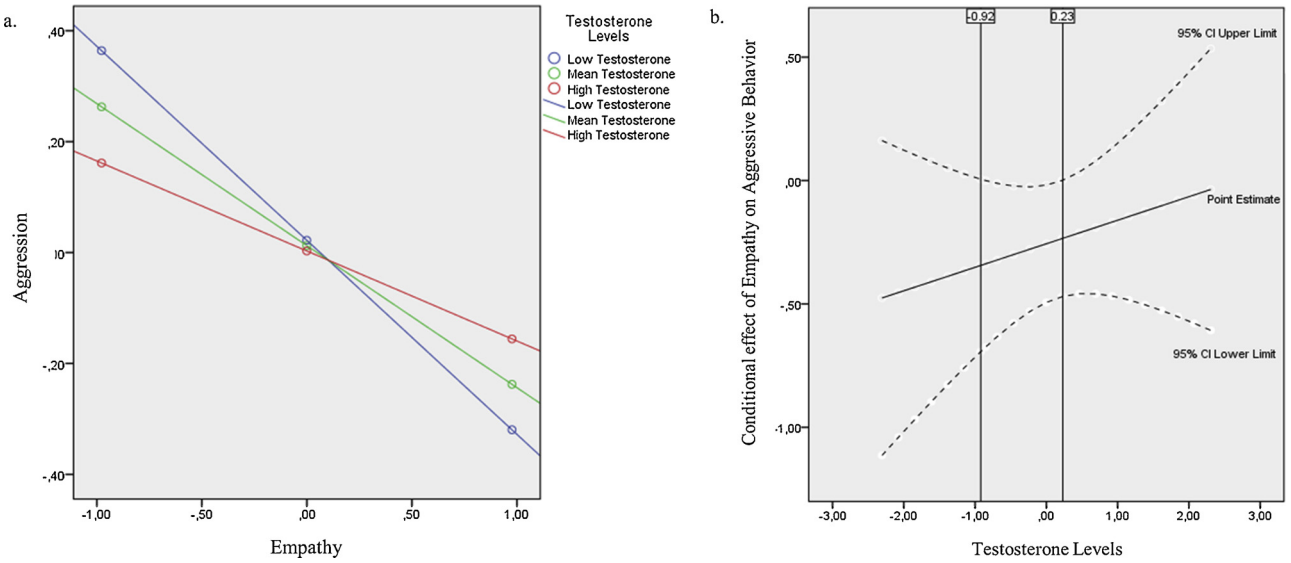

Fig. 1. a) Interaction between testosterone and empathy in relation to aggressive behavior in girls. b) Floodlight analysis graph of the conditional effect of Empathy on Aggression as a function of testosterone levels in girls.

sex and its interactions) to be analyzed, and in light of a previous study (Pascual-Sagastizabal et al., 2013) in which it was observed that aggressive behavior in boys and girls could be explained by different factors, the decision was made to replicate the same model separately for each sex. For boys, the model obtained was identical to that of the entire sample (R^2 = .22, $F_{(}7,72_{)}$ = 2.856, p = .011), while for girls, a new statistically significant interaction was found, in addition to the one mentioned earlier (R^2 = .36, $F_{(}7,51_{)}$ = 4.177, p = .001).

Specifically, in the regression analysis carried out for girls, a direct statistically significant effect was found for empathy and cortisol, and the interactions *testosterone x empathy* and *cortisol x empathy* were also found to be statistically significant. To analyze those interactions simple slopes tests were conducted as described above. First, the Johnson-Neyman technique was used to analyze the interaction between empathy and testosterone in girls. The visual plot of the interaction and floodlight analysis are shown in Fig. 1. The conditional effect of empathy on aggression is statistically significant when testosterone is between $M \geq$ -.92 and $M \leq$ .23, but not beyond those two values. That is, mean and low levels of testosterone influence the positive conditional effect of empathy on aggression. Secondly, the same approach was used to analyze the *cortisol x empathy* interaction. The visual plot of the interaction and floodlight analysis are shown in Fig. 2. The conditional effect of empathy on aggression is statistically significant when cortisol is between $M \leq$ -.92 and $M \geq$ -.14, but not beyond those two values. That is, mean and relatively high levels of cortisol influence the negative conditional effect of empathy on aggression.

In the regression analysis carried out for aggressive behavior in boys, a direct statistically significant effect was found for empathy, and the interaction *cortisol x empathy* was also found to be statistically significant. To analyze this interaction simple slope tests were conducted as described above. Thus, with the aim of analyzing the interaction between empathy and cortisol in boys the Johnson-Neyman technique was used. The visual plot of the interaction and floodlight analysis are shown in Fig. 3. The conditional effect of empathy on aggression is statistically significant when cortisol is greater than or equal to $M \geq$ -.48. That is, mean and high levels of cortisol influence the negative conditional effect of empathy on aggression for boys.

4. Discussion

The psychobiological approach proposed here constitutes a comprehensive view which takes into account the holistic functioning of the individual, analyzing whether interactions between biological and psychological variables are associated with aggressive behavior in school-aged children. In specific terms, the study analyzed the potential moderating role of salivary levels of testosterone, cortisol and estradiol on the attenuating effect of empathy on aggression among children of both sexes. The results obtained only partially confirmed our predictions. The *testosterone x empathy* interaction was associated with aggression in girls, with higher levels of empathy corresponding to lower levels of aggression at both low and mean testosterone levels. At high testosterone levels, however, aggression levels did not change. In other words, high empathy scores coupled with low and mean testosterone levels were associated with lower levels of aggression. This is consistent with the findings reported by previous studies, which observed a negative relationship between empathy and aggression (Berger et al., 2015; Euler et al., 2017; Garaigordobil and García, 2006) and a positive association between testosterone (and other androgens) and this type of behavior in boys (Barzman et al., 2013; Sánchez-Martín et al., 2000). However, the negative association found in our study between empathy and aggression disappeared when testosterone levels were high. The indicated relation might be due to the characteristics of the sample, taking into account that the research was conducted with school-age children, who were characterized by having low aggression and hormone levels. This may be the reason why although having obtained the expected negative relationship between the variables, it is only given at low and mean levels of testosterone. The aforementioned finding is important, as it shows that the relationship between empathy and aggression is moderated by testosterone levels, although only among girls, as the effect was not observed among boys. In a study carried out with 9-year-old children, Pascual-Sagastizabal et al. (2013) found that girls with high testosterone levels scored lower in cognitive empathy than their same sex age mates with low levels of this hormone. Moreover, girls with high testosterone levels were found to score similarly in this kind of empathy to boys with both low and high testosterone levels. Although in our study no negative association was observed between testosterone and empathy, in either boys or girls, it is also true that we did not measure cognitive empathy, which was the variable measured in the aforementioned study, as well as in the work of van Honk et al. (2011), who also found a negative association between this type of empathy and testosterone among young girls. As explained above, it has been suggested that in the EQ version it may be a cognitive factor (Lawrence et al., 2004) but the EQ-C provides a general empathy score. Therefore, we could not speak of a measure of cognitive empathy in the

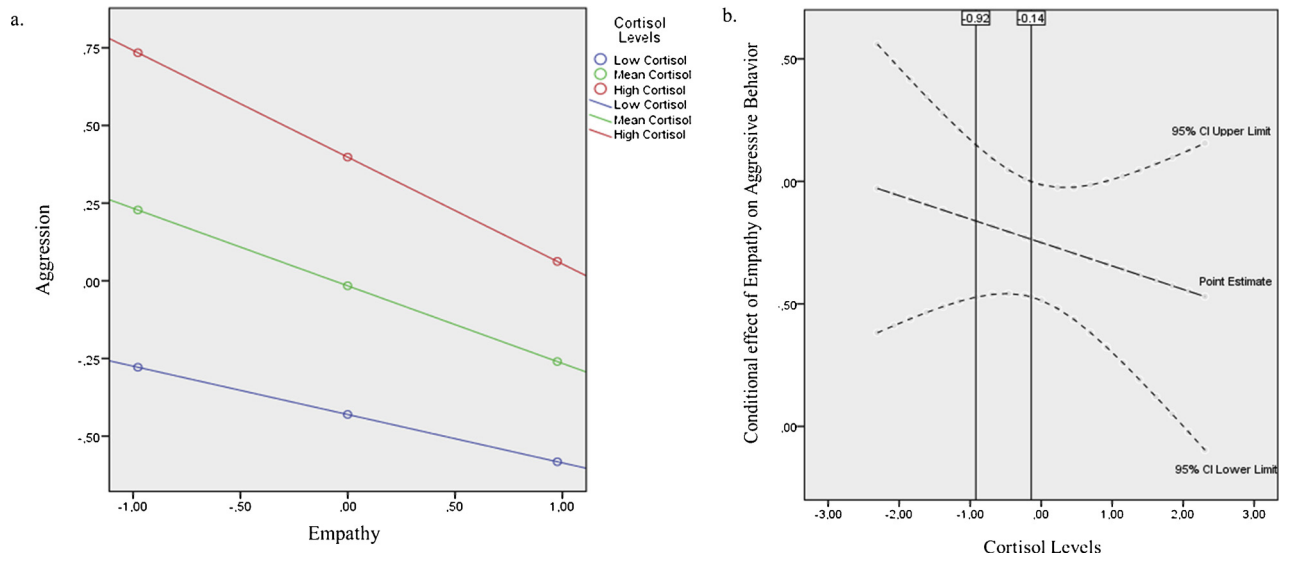

Fig. 2. a) Interaction between cortisol and empathy in relation to aggressive behavior in girls. b) Floodlight analysis graph of the conditional effect of Empathy on Aggression as a function of cortisol levels in girls.

test used in this study. The results of Pascual-Sagastizabal et al. (2013) and van Honk et al. (2011) may provide some clues as to how to interpret the results observed in this present study. It may be that high testosterone levels reduced the cognitive empathy of the girls in our study (which was something we did not measure), and although this did not affect their general empathy scores, it may nevertheless have decreased the attenuating effect of empathy on aggressive behavior. Furthermore, although no sex differences have been documented in relation to the attenuating effect of empathy on aggressive behavior, it is possible that high testosterone levels may inhibit this effect in girls.

But why in girls and not in boys? In order to gain control of resources, which is, in many cases, one of the main aims of aggression, boys often form coalitions with other boys - a strategy that is not so common among girls (Geary et al., 2003; Geary, 2010). Some authors have observed that the relationship between empathy and prosocial behavior, as well as between empathy and social acceptance, is stronger among boys than among girls (Braza et al., 2009; Roberts and Strayer, 1996), despite the fact that girls are generally more empathic than boys (Garaigordobil and García, 2006; Hoffman, 1977), as indeed was the case in our study. In relation to our results, this suggests that, in boys, the effects of testosterone and empathy on behavior would be independent of each other in relation to aggression, as high testosterone levels may foster dominance, and high levels of empathy may foster the social acceptance necessary to establish coalitions. Among girls, however, competition for access to resources does not generally result in the establishment of coalitions, which is why in agonistic contexts, the independence of the two factors (testosterone and empathy) may not be as necessary from an adaptive perspective as it is among boys. In this sense, it would be interesting to explore whether this interaction between testosterone and empathy plays a key role among girls with antisocial behavior problems.

In addition to the *testosterone x empathy* interaction discussed above, the *cortisol x empathy* interaction was associated with aggressive behavior in both boys and girls. In this sense, the results revealed that the relationship between empathy and aggression was moderated by mean and high cortisol levels. In other words, when cortisol levels were mean

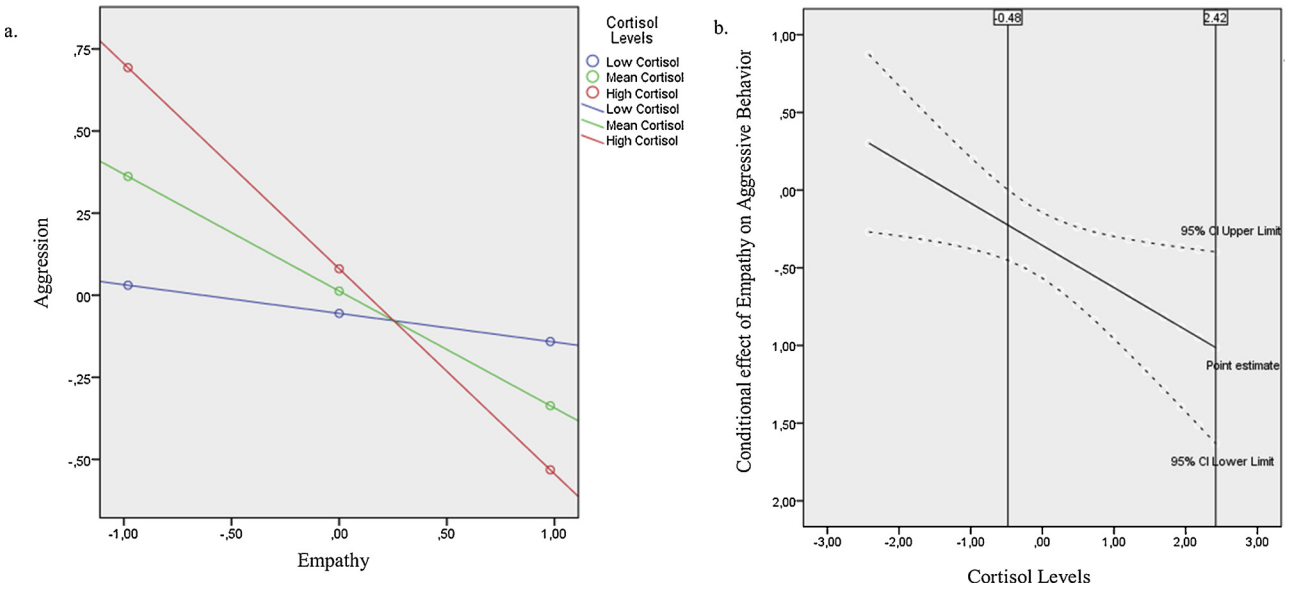

Fig. 3. a) Interaction between cortisol and empathy in relation to aggressive behavior in boys. b) Floodlight analysis graph of the conditional effect of Empathy on Aggression as a function of cortisol levels in boys.

and/or high, lower levels of empathy were found to correspond to higher aggression levels in boys, and higher levels of empathy to lower aggression levels in both boys and girls. In this case, the first part of the finding (i.e. the association between low empathy + mean/high cortisol and more aggression) is consistent with the positive relationship between aggression and cortisol levels found by several authors (Azurmendi et al., 2016; Böhnke et al., 2010; Lopez-Duran et al., 2009). The second part, however (i.e. the association between high empathy + mean/high cortisol and lower aggression levels) is consistent with the negative relationship observed between aggression and cortisol levels found by other authors (McBurnett et al., 2000; Virkkunen et al., 2004). Our results seem to reflect a complex set of interactions between cortisol and aggression, in which other factors also intervene, such as empathy, for example. These results can be interpreted as indicating that mean and high cortisol levels "reinforce" the negative association between empathy and aggression, with low empathy levels being linked to more aggression in boys, and high empathy levels to less aggression in both boys and girls. It is also possible that, in boys with low empathy levels, cortisol may provide the activation level necessary for coping with situations of conflict and competition in a more aggressive manner (Azurmendi et al., 2016). Indeed, some authors have observed an increase in cortisol levels in response to a situation of competition in which subjects prepare to attack (Suay et al., 1999), a finding which is consistent with the idea that higher cortisol levels help subjects cope with situations requiring intense energy expenditure (Mason et al., 1973). In less empathic subjects, a greater activation of the HPA axis fosters an aggressive response in order to help resolve conflicts. Our results show that when boys and girls have high empathy levels, mean and high cortisol levels are associated with less aggression. We should therefore consider the possibility that, in boys and girls with a greater capacity to emotionally connect with their peers, cortisol enhances this empathic ability, fostering a less aggressive response to social conflict; or perhaps more empathic subjects are simply more susceptible to the stressful situations generated by social interactions and conflicts- an idea which is consistent with that observed by Zilioli et al., (2015), who found that a combination of high cortisol and high testosterone levels was associated with more empathy. It is also consistent with that reported by Engert et al., (2014), who found an association between empathetic stress and cortisol reactivity. As Shirtcliff et al. (2009) argue: "*it may be that empathic/prosocial behaviors are supported by an optimal level of arousal reflected in moderately high cortisol levels and a corresponding level of internal distress that facilitates empathy (Eisenberg et al., 2007)*".

In our opinion, the main contribution made by this study is the fact that it demonstrates that analyzing the role of interactions between psychological and biological factors, as psychobiological markers, provides insight into the mechanisms that underlie aggressive behavior, which, like other behaviors, is characterized by its complexity and is based on an interlinking combination of psychological, biological and social factors which all act together (bio-psycho-social approach) to trigger it. The isolated analysis of these factors, while extremely useful, provides a less holistic view of the mechanisms underlying aggressive behavior. It is also important to take into account the specific way in which *hormone x psychological variable* interactions seem to act in boys and girls, as although no sex differences have been observed in aggressive behavior itself in the present study, this variable may be influenced by different psychobiological factors. In the future, it would be interesting to explore whether the interactions described affect boys and girls with antisocial behavior problems. Similarly, it would also be interesting to study the implications of this in the development of the psychopathy, taking into account that this study have been done with normative, non severe aggressive population, in which it has been suggested that both hormones and empathy may play an important role (Yildirim and Derksen, 2012). Furthermore, as regards real-world applications, the detection of psychobiological markers for aggression in children may constitute a useful tool for implementing preventive intervention strategies in early developmental stages, during which such strategies have proven to be more effective.

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Contributors

Author Pascual-Sagastizabal collected the data, undertook the statistical analysis and contributed in write manuscript. Authors Azurmendi and Cardas managed literature searches and collected data. Authors del Puerto and Vergara undertook the statistical analysis and contributed to discussion of the results. Author Sánchez-Martín designed the study and wrote the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors report no conflict of interest.

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