Sex hormone receptor expression in children with autism spectrum disorder

Ruoyu Sun
Foshan Maternal and Child Health Hospital, Southern Medical University

Pi Guo
Shantou University Medical College

Tao Sun
Foshan Maternal and Child Health Hospital, Southern Medical University

Hong Yu
Foshan Maternal and Child Health Hospital, Southern Medical University

Yanwei Liao
Foshan Maternal and Child Health Hospital, Southern Medical University

Jieqi Xie
Foshan Maternal and Child Health Hospital, Southern Medical University

Jiaying Zeng
Foshan Maternal and Child Health Hospital, Southern Medical University

Xiaoyun Xie
Foshan Maternal and Child Health Hospital, Southern Medical University

Saijun Huang (✉ huangsaijun2011@163.com)
Foshan Maternal and Child Health Hospital, Southern Medical University

Research Article

Keywords: Autism spectrum disorder, Estrogen receptor β, Androgen receptor, Progesterone receptor

Posted Date: January 3rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2345028/v1

License: ☃️ This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Background

Sex hormones, especially estrogen, which binds to estrogen receptor β (ERβ), play a vital role in the pathogenesis of mental disorders such as autism spectrum disorder (ASD). The purpose of this study was to analyze the serum levels of hormone receptors, including ERβ, progesterone receptor (PGR) and androgen receptor (AR), and compare these levels between children with ASD and typically developing (TD) children. We also investigated the relationships of ERβ mRNA levels with ASD core symptoms, sleep, and developmental quotients (DQs) from the Gesell Developmental Schedules (GDS) among children with ASD.

Methods

We compared the mRNA levels of ERβ, AR, and PGR between 56 children with ASD and 37 TD children by using quantitative real-time PCR. Then, a correlation analysis was performed to determine the correlations of ERβ mRNA levels with Childhood Autism Rating Scale (CARS), Autism Behavior Checklist (ABC), and Children’s Sleep Habits Questionnaire (CHSQ) scores as well as DQs among ASD children.

Results

We found that serum mRNA levels of ERβ in ASD children were significantly lower than those in the TD group. However, we found no correlations of the ERβ mRNA level with CARS, ABC, and CHSQ scores as well as DQs on each GDS domain among ASD children.

Conclusions

Elevated ERβ mRNA levels in peripheral blood may be related to ASD but this association needs to be validated with a larger sample size.

1. Introduction

Autism spectrum disorders (ASD) are a group of neurodevelopmental disorders characterized by impairments in social communication, the presence of restricted or repetitive behaviors, or both (Randall M, et al., 2018). The prevalence of ASD exhibits a clear sex difference, with a male/female ratio of 4.2:1, suggesting a potential role of sex hormones in the pathogenesis of this disorder (Maenner MJ, et al., 2021). Researchers have argued that exposure to high intrauterine levels of testosterone in early development is a risk factor for ASD (Ferri SL, et al., 2018). The positive association between fetal testosterone levels and autistic features has also been confirmed (Ingudomnukul E et al., 2007). Additionally, testosterone is an important stimulant of prostate cell proliferation; therefore, several biological processes directly influenced by androgens and estrogens, such as through estrogen receptors alpha (ERα) and beta (ERβ) (Gardner MJ et al., 1987; Cohen DW et al., 1994). Recent studies have shown that suppression of ERβ and its target gene is associated with ASD development; in contrast, the expression of ERα has little correlation with ASD (Zou Y et al., 2017; Li L et al., 2018; Xie W et al., 2018). These findings suggest that prenatal androgen exposure may induce ASD development by suppressing ERβ. Recently, a study showed that prenatal dihydrotestosterone exposure induces autism-like behavior in mice through androgen receptor (AR)-mediated suppression of ERβ; prenatal and postnatal treatment with berberine ameliorated this effect by suppressing ARs (Xiang D et al., 2020). In addition, studies have suggested...
that autism is associated with immune-mediated events during early brain development (Patterson PH et al., 2009; Patterson PH et al., 2011). Progesterone helps to regulate immune function and protect the brain from the damaging effects of infections and inflammation (Lee JH et al., 2011). This evidence suggests that the sex differences in ASD may arise from the effects of sex hormones on brain development.

There is no quantitative method for early ASD screening or to predict the risk of ASD. Additionally, to the best of our knowledge, no study to date has examined ERβ levels in the peripheral blood of ASD patients. Therefore, this study explored ERβ mRNA levels in the peripheral blood of children with ASD. To investigate the relationship between ERβ levels and brain functions, we analyzed the correlations of ERβ mRNA levels with ASD-related scale scores, sleep quality, and developmental quotients (DQs) from Gesell Developmental Schedules (GDS) among ASD children.

2. Methods

2.1 Participants

A total of 56 children diagnosed with ASD according to the Statistical Manual of Mental Disorders, fifth edition (DSM-V), from 2018 to 2020 at the Department of Child Health, Foshan Maternal and Child Health Hospital, Southern Medical University were enrolled in this study. The age of the ASD children was 2.68 ± 0.67 (mean ± standard deviation [SD]) years. During the same period, 37 typically developing (TD) children were recruited as the comparison group. The age of the TD children was 3.20 ± 0.83 years. TD children underwent mental and neurological examinations and were free of developmental disorders and nervous system diseases. All enrolled children were between the ages of 2 and 5 years old. Peripheral blood was collected from all subjects. All families signed informed consent forms before participation. This study was approved by the Ethics Committee of Foshan Maternal and Child Health Hospital.

2.2 RT-qPCR

The detection procedure was described in a previous study (Li S et al., 2018). Total RNA was extracted from peripheral blood using an Easy Pure RNA Kit (TransGen Biotech, Beijing, China). The quality and quantity of RNA were measured using a Nanodrop-2000 (Thermo Fisher Scientific, USA). Two-step real-time polymerase chain reaction (PCR) was performed with TransStart Tip Green qPCR SuperMix according to the manufacturer’s instructions on a LightCycler96 (Roche Diagnostics Ltd, Rotkreuz, Switzerland). Quantitative PCR (qPCR) was performed with a 30 s at 95°C, followed by 40 cycles of 95°C for 5 s, 55°C for 15 s and 72°C for 10 s. The relative expression of genes was normalized to the expression of GAPDH using the 2-ΔΔCT method.

2.3 ASD symptoms, sleep, and development quotients

The ASD and TD groups completed a clinical information questionnaire. All groups competed a GDS assessment to evaluate neurological development and the Children's Sleep Habits Questionnaire (CSHQ) to assess sleep. The ASD group also completed the Childhood Autism Rating Scale (CARS) and the Autism Behavior Checklist (ABC) to evaluate ASD symptoms.

The CARS and the ABC are used for the clinical diagnosis and evaluation of ASD symptoms. Specifically, the CARS is used to determine the severity of ASD symptoms, with a CARS score of 30 to 36 indicating mild-to-moderate autism symptoms and a CARS score of 37 to 60 indicating severe autism symptoms (Duan G et al., 2014). The ABC is a 57-item screening checklist for autism that is designed to be completed during parent interviews. The CARS and ABC demonstrate good reliability and validity in China (Lu J et al., 2004).

The CSHQ is a parent-report instrument used to examine sleep habits and identify sleep problems (Owens JA et al., 2000). The CSHQ contains eight subscales: bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night
waking, parasomnias, sleep-disordered breathing, and daytime sleepiness. Higher scores indicate more disturbed sleep. This questionnaire has been used to evaluate sleep in preschoolers with and without ASD (Goodlin-Jones BL et al., 2008).

GDS divide children's neurodevelopment into five domains, namely, adaptability, gross motor skills, fine motor skills, language and personal-social skills (Dror R et al., 2009). The DQ on each of the five domains is used to evaluate the level of neurodevelopment. The higher the DQs are, the better the neurodevelopment.

### 2.4 Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS 25.0) software. The continuous variables are expressed as the mean ± SD. Frequencies with percentages are reported for categorical variables. Differences in categorical variables between the ASD and TD groups were tested using the chi-square test. Differences in continuous variables between the ASD and TD groups were tested using two independent-sample t tests or Wilcoxon rank–sum tests. We used analyses of variance (ANOVAs) or Kruskal–Wallis H tests to determine the differences between the ASD subgroups and the TD group. A Pearson correlation analysis was used to analyze normally distributed variables. For all analyses, statistical significance was set at a $P$ value of 0.05.

### 3. Results

#### 3.1 Clinical characteristics

The demographic and clinical characteristics of 56 ASD children and 37 TD children are shown in Table 1. In the ASD group, there were more males ($n = 50, 89.3\%$) than females ($n = 6, 10.7\%$) (Table 1), but the sex difference between the ASD and TD groups was not statistically significant. The numbers of ASD children with mild-to-moderate and severe ASD were 38 (68\%) and 18 (32\%), respectively, as evaluated by the CARS. In addition, there were also no significant differences between the two groups in terms of maternal age, medication during pregnancy, second-hand smoke exposure during pregnancy or experience of disease during pregnancy.
Table 1  
Characteristics of typical developing children and ASD patients.

<table>
<thead>
<tr>
<th>Index</th>
<th>TD group (n = 37)</th>
<th>ASD group (n = 56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td>0.646</td>
</tr>
<tr>
<td>Male</td>
<td>31 (83.8)</td>
<td>50 (89.3)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6 (16.2)</td>
<td>6 (10.7)</td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mild-to-moderate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>3165 ± 726</td>
<td>3228 ± 588</td>
<td>0.290</td>
</tr>
<tr>
<td>Maternal age, years</td>
<td>29.41 ± 4.17</td>
<td>28.39 ± 4.89</td>
<td>0.393</td>
</tr>
<tr>
<td>Medication during pregnancy</td>
<td></td>
<td></td>
<td>0.098</td>
</tr>
<tr>
<td>Yes</td>
<td>5 (13.51)</td>
<td>4 (7.14)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>32 (86.49)</td>
<td>52 (92.86)</td>
<td></td>
</tr>
<tr>
<td>Second-hand smoke exposure during pregnancy</td>
<td></td>
<td></td>
<td>0.307</td>
</tr>
<tr>
<td>Yes</td>
<td>3 (8.11)</td>
<td>10 (17.86)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34 (91.89)</td>
<td>46 (82.14)</td>
<td></td>
</tr>
<tr>
<td>experience of disease during pregnancy</td>
<td></td>
<td></td>
<td>0.230</td>
</tr>
<tr>
<td>Yes</td>
<td>24 (64.86)</td>
<td>28 (50.00)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13 (35.14)</td>
<td>28 (50.00)</td>
<td></td>
</tr>
</tbody>
</table>

A total of 93 subjects were examined. P value for comparison between two groups are calculated by t-tests or Chi-square test. TD typical developing, ASD autism spectrum disorder.

3.2 mRNA levels of ARs, PGRs, and ERβ in the peripheral blood of ASD children

To analyze the mRNA levels of potential biomarkers for ASD (progesterone receptors [PGRs], androgen receptors [ARs] and ERβ) in the peripheral blood of TD and ASD subjects, RT-qPCR was performed. As shown in Fig. 1, ERβ mRNA levels were significantly lower in the ASD group than in the TD group (P = 0.026, P < 0.05), while the AR and PGR mRNA levels did not significantly differ between the two groups (P > 0.05) (Fig. 1). We also conducted a subgroup analysis of ERβ mRNA levels in children with different degrees of ASD severity as well as TD subjects. We found that ERβ mRNA levels did not significantly differ among the mild-to-moderate ASD, severe ASD, and TD groups (P > 0.05) (Fig. 2).

3.3 Evaluation of ASD symptoms, sleep and DQs
As shown in Table 2, ASD children had more disturbed sleep than TD children according to the CSHQ ($P = 0.009$). In addition, the ASD group had lower GSD DQs than the TD group ($P = 0.002$).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>ASD symptoms, sleep evaluation and development quotients between typical developing children and ASD children.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TD group (n = 37)</td>
</tr>
<tr>
<td>CHSQ</td>
<td>47.28 ± 4.94</td>
</tr>
<tr>
<td>GDS</td>
<td>95.65 ± 8.06</td>
</tr>
<tr>
<td>CARS</td>
<td>37.55 ± 4.78</td>
</tr>
<tr>
<td>ABC</td>
<td>82.64 ± 31.86</td>
</tr>
</tbody>
</table>

A total of 93 subjects were examined. Values are mean ± SD. $P$ value for comparison between two groups are calculated by t-tests. TD typically developing, ASD autism spectrum disorder. CHSQ Children's Sleep Habits Questionnaire, GDS Gesell Developmental Schedules, CARS Childhood Autism Rating Scale, ABC Autism Behavior Checklist.

3.4 Pearson correlation analysis of ERβ mRNA levels, ASD symptoms, sleep and DQs

Pearson correlation analysis revealed that the ERβ mRNA levels in children with ASD were not correlated with total scores on the CARS, ABC, or CHSQ or DQs on any of the domains (adaptability, gross motor skills, fine motor skills, language and personal-social skills) ($r = -0.01$, -0.15, -0.03, -0.10, -0.06, -0.10, -0.12, -0.17 and −0.04, respectively; $P = 0.94$, 0.26, 0.83, 0.47, 0.66, 0.48, 0.39, 0.23, and 0.80, respectively) of the GDS. The details are shown in Table 3.
<table>
<thead>
<tr>
<th></th>
<th>ER(\beta)</th>
<th>CARS</th>
<th>ABC</th>
<th>CHSQ</th>
<th>DQ</th>
<th>adaptability</th>
<th>gross motor</th>
<th>fine motor</th>
<th>language</th>
<th>personal-social behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER(\beta)</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CARS</td>
<td></td>
<td>-0.01</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td></td>
<td>-0.15</td>
<td>0.65</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHSQ</td>
<td></td>
<td>-0.03</td>
<td>0.01</td>
<td>-0.58</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DQ</td>
<td></td>
<td>-0.10</td>
<td>-0.54</td>
<td>-0.28</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adaptability</td>
<td></td>
<td>-0.06</td>
<td>-0.47</td>
<td>-0.22</td>
<td>-0.01</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gross motor</td>
<td></td>
<td>-0.09</td>
<td>-0.34</td>
<td>-0.116</td>
<td>-0.12</td>
<td>0.83</td>
<td>0.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fine motor</td>
<td></td>
<td>-0.19</td>
<td>-0.34</td>
<td>-0.09</td>
<td>-0.93</td>
<td>0.81</td>
<td>0.76</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>language</td>
<td></td>
<td>-0.17</td>
<td>-0.58</td>
<td>-0.58</td>
<td>0.16</td>
<td>0.79</td>
<td>0.54</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>personal-social behavior</td>
<td></td>
<td>-0.04</td>
<td>-0.46</td>
<td>-0.32</td>
<td>-0.01</td>
<td>0.84</td>
<td>0.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ER\(\beta\) estrogen receptor \(\beta\), CHSQ Children's Sleep Habits Questionnaire, GDS Gesell Developmental Schedules, CARS Childhood Autism Rating Scale, ABC Autism Behavior Checklist. \(r\) correlation coefficient, \(P\) for comparison between two subjects are calculated by Pearson correlation.
4. Discussion

To the best of our knowledge, no previous studies have reported a difference in Erβ mRNA levels in peripheral blood between ASD and TD children. In the present study, we showed that the ERβ mRNA levels in the peripheral blood of ASD children were significantly lower than those in the TD group. Additionally, ASD children had a higher score than TD children on the CSHQ, indicating that ASD children have more disturbed sleep.

Our findings were consistent with a recent study that reported that lower ERβ levels contributed to the development and progression of ASD and that upregulated ERβ expression attenuated this effect (Xie W et al., 2018; Zou Y et al., 2017). Currently, the exact cause and mechanisms of ASD are still unclear, but genetic and environmental factors are believed to jointly mediate its pathogenesis (Goines PE et al., 2013). Numerous experimental studies have demonstrated that chronic neuroinflammation, imbalance of excitatory and inhibitory neurotransmission, mitochondrial dysfunction and oxidative stress are important factors in the pathogenesis of ASD (Young AM et al., 2011; Quiñones-Camacho LE et al., 2021; Morgan JT et al., 2010; Vargas DL et al., 2005). Abnormal regulation of sex hormones is also involved in the pathogenesis of ASD, as there are obvious sex differences in ASD patients (Berkel S et al., 2018). A study in 2020 showed that latent prenatal steroidogenic activity was elevated in the amniotic fluid of autistic boys, which suggests that prenatal estrogens contribute to the risk of ASD (Baron-Cohen S et al., 2020). By activating ERβ, estrogen influences cognition, learning and memory by affecting the development of neurons, formation of synapses, development of circuits and other important variables during brain development (Nalvarte I et al., 2021). ERβ is known to mediate some of the effects of estrogens on behaviors not specifically associated with reproduction, such as locomotor activity, fear responses, anxiety, and learning (Goines PE et al., 2013). Additionally, ERβ knockdown abolished E2-induced reductions in depressive behavior in mice (Altun H et al., 2017). Moreover, administration of ERβ agonists or selective ligands reduced anxiety-like behavior and depressive behavior in rats (Weiser MJ et al., 2010).

In this study, we found a higher proportion of males (89.3%) than females (10.7%) among ASD children. Moreover, serum ERβ levels were significantly lower in ASD children than in TD children; however, the ERβ, AR and PGR mRNA levels did not significantly differ among the TD, mild-to-moderate ASD and severe ASD groups. An animal trial showed that endogenous (progesterone) or synthetic progestin (norethindrone)-exposed offspring both exhibited autism-like behavior, which demonstrated that prenatal progestin exposure may induce ASD (Li L et al., 2018). Another study showed that overexpression of an AR-dependent gene in conjunction with that of DNA methyltransferase, which methylates oxytocin receptors, delivered high arousal inputs to the amygdala, resulting in aberrant socialization, a key characteristic of autism (Mbadiwe T et al., 2013). Although our results were somewhat different from those of other studies, the use of AR and PGR mRNA levels for differentiating between ASD and TD populations merits further exploration.

A previous study reported that sleep problems and ASD do not have a bidirectional association. Sleep problems co-occur with autistic traits in early childhood. The authors suggested that sleep problems are part of the ASD construct (Verhoeff ME et al., 2018). Similarly, we found that ASD children had more disturbed sleep than TD children according to CHSQ scores. In addition, we found that TD children had higher GDS DQs than ASD children, which may be associated with the inclusion requirements of the TD group. However, we found no correlations of ERβ mRNA levels in children with ASD and total scores on the CARS, ABC, or CHSQ or GDS DQs. We did not find significant modifications of clinical characteristics in these associations.

There are some advantages in our study. First and foremost, most previous studies on this subject have focused on animal models rather than humans. Second, some investigations have confirmed that the expression of ERβ in the brain is reduced in ASD children compared with TD children; this study is the first to characterize and ERβ mRNA levels in peripheral blood samples from ASD children. In addition, professional screening and diagnosis procedures ensured
the reliability of our results. However, our study has several limitations. This was a case–control study, and causality could not be inferred. In the future, we plan to use a cohort design to clarify causality. Additionally, although we found a reduction in ERβ mRNA levels in peripheral blood, we were unable to determine the potential mechanism or conduct dose–response analyses.

As estrogens promote the survival of nerve cells and reduce neuronal damage, researchers have argued that estrogens may ameliorate the symptoms of ASD (Cheng D et al., 2014). Our data indicates that ERβ may play an important role in the etiology of ASD. This relationship should be validated with a larger sample size.

5. Conclusion

In summary, we found a significant difference in the ERβ mRNA level in peripheral blood between ASD children and TD children, indicating potential biomarkers for differentiating between ASD and TD populations. Our findings suggest that ERβ is involved in the development of ASD, but the relationship between ERβ and ASD needs to be further investigated.

Declarations

Funding

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

Availability of data and materials

All data generated or analysed during this study are included in its supplementary information files.

Acknowledgements

Not applicable.

Consent to Publish

Not applicable.

Authors Contributions

Conceptualization: RYS, SJH, and PG. Data curation: RYS, TS, JQX, HY, and SJH. Formal analysis: RYS, and PG. Investigation: YWL, TS, JQX, and XXY. Methodology: JYZ, RYS, and SJH. Project administration: RYS, HY, and SJH. Roles/ Writing- original draft: RYS, and TS. Writing - review & editing: PG, JYZ and SJH.

Ethical Approval

The study was approved and consent to participate by the Foshan Maternity and Child Health Hospital Ethics Committee (Approval Number: FSFY-MEC-2020-021). All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were approved by Foshan Maternity and Child Health Hospital Ethics Committee.

Human Ethics
All families signed informed consent forms before participation. This study was approved by the Ethics Committee of Foshan Maternal and Child Health Hospital.

References

Figure 1

The mRNA levels of AR, PGR and ERβ between TD group and ASD group. ERβ mRNA levels were significantly lower in ASD group than in TD group ($P = 0.026, P < 0.05$), while the mRNA levels of AR and PGR were no significant difference between two groups ($P > 0.05$).
Figure 2

The mRNA levels of AR, PGR and ERβ among TD group, moderate-to-severe ASD group and severe ASD group. The mRNA levels of AR, PGR and ERβ were no significant difference among moderate-to-severe, severe of ASD and TD group ($P>0.05$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- rawdata.pdf