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Original Article

Physiology Section

Auditory and Visual Reaction Time in Polycystic Ovarian Syndrome

RUPALI MEHTA[1], MANJINDER KAUR[2], POOJA GANDHI[3], PRIYANKA PARIHAR[4]

ABSTRACT

Introduction: Polycystic Ovarian Syndrome (PCOS) is a hormonal disorder of female reproductive system causing infertility, irregular menstrual cycle and hormonal imbalance characterised by hyperestrogenemia, hyperprolactinemia, increased Anti Mullerian Hormone (AMH) and Thyroid Stimulating Hormone (TSH). Apart from the role in female reproductive system, these hormones are shown to have neuromodulatory role, affecting the neuronal activity. Thus, the auditory and visual reaction time may be affected in the women with polycystic ovaries.

Aim: To evaluate the auditory and visual reaction time, in patients with polycystic ovarian syndrome.

Materials and Methods: The study was designed as a case-control study where the 80 otherwise healthy women, attending infertility OPD, were recruited for the study and divided into groups viz., PCOS (n=40) and NPCOS (n=40).

The subjects from both the groups were evaluated for their anthropometric data, hormone levels {Serum estrogen, Serum prolactin, Serum TSH, Serum AMH} using COBAS-6000 analyser along with the auditory and visual reaction time using RTM-608 (Medicaid). The observations were recorded and analysed using paired t-test.

Results: Auditory reaction time had significantly decreased (p=0.012) while visual reaction time was non-significantly reduced in Group PCOS as compared to Group NPCOS.

Conclusion: The altered hormonal profile in PCOS i.e., hyperestrogenemia and hyperprolactinemia exerts enhanced neuromodulatory action through neural ERα receptors and tuberoinfundibular dopaminergic neurons in hypothalamus, thus resulting in increased neuronal excitability and decreased reaction time in patients with PCOS.

Keywords: Anti mullerian hormone, Prolactin, Reaction time

INTRODUCTION

PCOS is a condition in which women experiences various physiological, genetic as well as environmental changes. It is a hormonal disorder causing enlarged ovaries with many small cysts. Globally, PCOS is affecting many women in their reproductive age in an inconstant manner and this variable prevalence of PCOS is been observed as 2-25% [1]. The wide range of ubiquity of PCOS is might be due to disparate presentation of symptoms, diagnostic standards. Onset of PCOS occurs at the early age in girls when they start menstruating [1]. PCOS includes wide spectrum of clinical symptoms which are mainly caused by androgens resulting in increased BMI in women. It is known to have a multi factorial origin like infertility, menstrual disorder, elevated insulin level, hyperandrogenemia associated with obesity, increased BMI, type 2 diabetes, heart disease, mood disorder, obstructed sleep apnoea, endometrial cancer, hypothyroidism, hyperprolactinemia, hyperlipidemia, anovulation, altered cognitive functions of the brain etc., [2].

The patients of PCOS are generally obese with Body Mass Index ranging from 25 to 29.9 kg/m^2 which has direct effect on estradiol metabolism due to which there is a disturbance in the female reproductive cycle. Though estradiol is primarily a reproductive hormone but it has been shown to alter the neuronal excitability. The excitatory and inhibitory effect of neurons due to hormonal variation in PCOS patients possibly results in alteration in responses to various reactions [3].

Reaction to any stimulus is a voluntary response which is measures the speed of response of a person. Process of responding tostimuli involves stimulus processing, decision making, attention span and response programming [4].

From previous studies, it is apparent that reaction time is the depiction of the neural integrity. It has also been seen that visual reaction time is increased in luteal phase (due to progesterone) as compared to follicular phase (due to estradiol) where increased neuronal conduction was attributed to oestrogenic influence and thereby decreasing the reaction time [5].

Hence, these findings triggered this study, i.e., to find out the effect of the deranged hormone profile in PCOS, on the neuronal activity of women, which could be measured indirectly through the reaction time assessment, for which the auditory and visual reaction times were chosen. Thus, the present study was designed with an aim to evaluate the neuronal activity through auditory and visual reaction time in patients with Polycystic ovarian syndrome.

MATERIALS AND METHODS

The present study was designed as a comparative case-control study, which was started only after obtaining ethical clearance from institutional ethical committee. The written consent was taken from the study participants. The cases were recruited from the fertility centre of Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India, by random sampling. The data collection for the study took four months to get completed i.e., from March 2016 to July 2016.

The study was conducted on 80 women who were divided equally into two groups; PCOS and NPCOS. The sample size was calculated from the formula:

$$n=4pq/L^2$$

where, p=10.32; (prevalence of PCOS calculated from a previous study), q=100-p=89.8; (with 10% permissible error, L); n=4×10.32×89.8/100=37.06, rounded off to 40, in each group [1,2].

The patients in Group PCOS included 40 healthy women with PCOS; Group NPCOS included 40 healthy women without PCOS, attending the infertility OPD and consented to participate in study. Both the groups were compared for various anthropometric and vital parameters and were matched for age, height, Body Mass Index (BMI), heart rate, blood pressure.

Patients were diagnosed according to AES criteria (2010); [1,6] which states that a woman is diagnosed as PCOS when all three of the following criteria are present:

1. Hyperandrogenism (clinical or biochemical)
2. Ovarian dysfunction (oligomenorrhoea or anovulation and/or polycystic ovarian morphology)
3. Exclusion of other androgen excess or related disorders

However, the subjects with any other systemic disease except PCOS were excluded from the study.

After a detailed physical examination, the anthropometric measurements were obtained of all the participants, viz. height, weight and BMI.

The blood samples (5 mL) was taken, from all the subjects for various biochemical parameters, viz., Random Blood Sugar (RBS), hormonal status (serum estradiol, serum prolactin, serum Anti Mullerian Hormone (AMH) and serum Thyroid Stimulating Hormone (TSH) and were measured using fully automated COBAS-6000 analyser based on principle of chemiluminiscence.

The audio-visual reaction time, of the participants from both the groups was measured using audio visual reaction time machine (RTM-608 and supplied by Medicaid Chandigarh). This instrument is equipped with a sensitive quartz clock which measured upto 1/10th of a msec with an accuracy of +1 and -1 digit. The audio-visual reaction time was measured in a quiet room of Fertility department of our hospital. Each session lasted for about 15 minutes. A practice session was given to the subjects before starting the test.

All the subjects used their dominant hand to press the switch to stop the quartz clock of the apparatus. Before measuring the visual reaction time, each subject was asked to respond to the alternating flashing of the red, green and yellow light. They were instructed to press the corresponding switch as soon as they see the light. This process was repeated for about nine times.

For measuring auditory reaction time, they were asked to respond a total of nine auditory stimuli of varied frequencies (250 Hz, 500 Hz and 750 Hz) by pressing the corresponding switch immediately to stop the sound.

All the readings for Auditory Reaction Time-Visual Reaction Time (ART-VRT) were recorded for the respective groups. Each auditory and visual stimulus was given thrice and the average of all these stimuli was recorded as mean ART/VRT.

STATISTICAL ANALYSIS

The data collected were analysed using unpaired t-test; and p-value <0.05 was considered as significant.

RESULTS

[Table/Fig-1] shows that there is no significant difference in mean age, mean height, weight and BMI in both the groups. Also, the heart rate, blood pressure and random blood sugar level were comparable and showed no significant difference among both the groups.

Parameters	Group PCOS	Group NPCOS
Mean Age (years)	27±5.24^{NS}	30.5±6.2
Mean Height (cm)	2.3±0.15^{NS}	2.4±0.16
Mean Weight (kg)	52.9±10.9^{NS}	55.2±10.4
Mean Body Mass Index (kg/m^2)	22.2±5^{NS}	22.6±4.4
Mean Heart Rate (beats/minute)	82.5±15.7^{NS}	80.3±10.9
Mean Systolic Blood Pressure (mm/Hg)	109.1±14.8^{NS}	118±13.4
Mean Dystolic Blood Pressure (mm/Hg)	72.3±12.6^{NS}	78.5±10.10
Mean Random Blood sugar (mmol/L)	5.8±5.5^{NS}	5.5±1.3

[Table/Fig-1]: Comparative values of various anthropometric and vital parameters in both the groups.
NS-not significant as assessed by unpaired t-test

On the other hand, the hormone levels (mean serum AMH, mean serum prolactin, mean serum AMH and mean serum estradiol) were significantly (p<0.01) elevated in Group PCOS as compared to Group NPCOS. However, serum TSH was non-significantly lower in the test group [Table/Fig-2].

Parameters	Group PCOS	Group NPCOS
Serum AMH (ng/mL)	5.20±1.36*	1.54±1.19
Serum Estradiol (pg/mL)	21.09*	5
Serum Prolactin (ng/mL)	19.23±9.9*	14.15±6.57
Serum TSH (µL/mL)	3.03±2.3^{NS}	3.3±3.15

[Table/Fig-2]: Mean values of AMH, Prolactin and TSH; mean value of Estradiol in both the groups.
*p<0.01, highly significant; NS: Non Significant as assessed by unpaired t-test
These hormonal tests were done by collecting blood samples of the volunteers and were measured using COBAS-6000 analyser.

The ART for group PCOS was significantly lower (p=0.012) as compared to the other group whereas VRT was non-significantly lower in PCOS group [Table/Fig-3].

Parameters	Group PCOS	Group NPCOS
ART (msec)	1.18±0.4*	1.38±0.36
VRT (msec)	0.86±0.26^{NS}	0.91±0.2

[Table/Fig-3]: Mean ART and VRT in both the groups.
*p=0.012, highly significant; NS: Non Significant by unpaired t-test
The Auditory Reaction Time and Visual Reaction Time was measured using RTM-608 (Medicaid, Chandigarh).

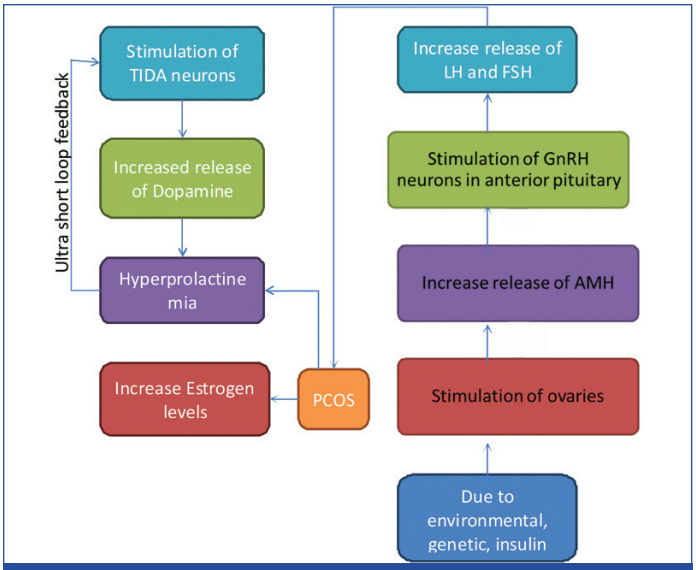
DISCUSSION

The present study documents a significant decrease in auditory reaction time whereas non significant decrease in visual reaction time in patients with PCOS as compared to non PCOS. It was also observed that the decrease in ART was 14.49% and 5.49 % in VRT, for group PCOS when compared to group NPCOS. The decreased reaction time in group PCOS could be attributed to altered hormonal profile in the patients with PCOS.

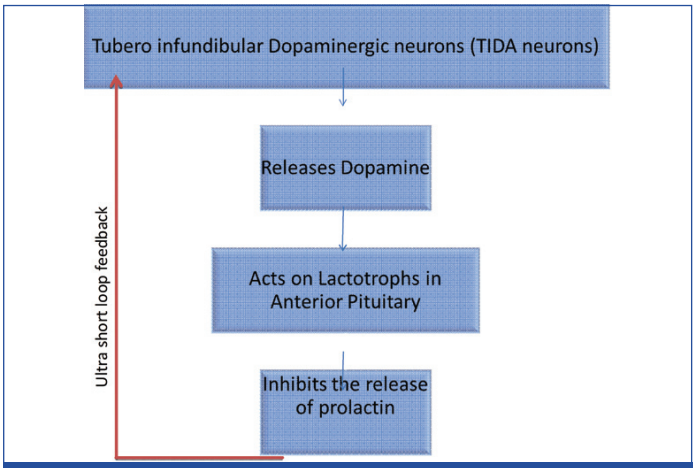
As observed in [Table/Fig-2], the various hormones viz., serum estradiol, serum prolactin and serum AMH were significantly high in the study group (Group PCOS) indicating the interplay of these hormones in modulating the neuronal activity, hence affecting the reaction time. These hormones are documented to have varied effects on neuronal activity of brain [7].

Various environmental and genetic factors along with physical inactivity results in obesity and insulin resistance in PCOS, prevalently seen nowadays, hence stimulates the ovaries causing an increase in release of AMH. The AMH has been reported to have a stimulatory effect on Gonadotrophin releasing hormone neurons, located in hypothalamus, which secrete high amount of gonadal hormones (Luteinizing hormone and Follicle Stimulating Hormone) causing an increase in follicular growth and ovarian hyperandrogenemia resulting in PCOS [7,8]. As a result, PCOS causes hyperestrogenemia and hyperprolactinemia. The literature has clearly indicated the neuroexcitatory role of estradiol through ERα receptors [5]. The hyperprolactinemia, seen in PCOS may occur directly through hyper ovaries or indirectly through raised estradiol levels [9]. The studies have also reported that a high level of prolactin stimulates Tubero Infundibular Dopamine (TIDA) neurons through ultra short loop feedback mechanisms. Stimulation of TIDA neurons results in high Dopamine levels, which is also a neuromodulatory neurotransmitter [Table/Fig-4] [9]. Hyperprolactinemia has also been reported to result in natriuresis, diuresis and kaliuresis thus altering the fluid and electrolyte balance of the body [10]. This electrolyte imbalance may affect the membrane potential and hence neuronal activity [Table/Fig-5].

The altered hormonal profile, during pregnancy has also documented the increased reaction time, mainly attributed to progesterone [11].



[Table/Fig-4]: Excitatory effect of prolactin on TIDA neurons.



[Table/Fig-5]: Hormonal variation in PCOS.

The present study has also reported the significant hyperprolactinemia in Group PCOS, which might mediate its effects through Dopaminergic neurons on anterior pituitary gland. Levels of dopamine are found to influence various neuronal responses such as auditory responses, integration, attention, physiological state and neuronal disorders [12].

Another insignificant finding in both the groups was the normal levels of TSH, though the levels were in high normal range. The literature has documented a close association of sub clinical hypothyroidism with PCOS, which was not seen in this study [13]. As documented raised TSH level could prolong the reaction time but in this study the levels of TSH were normal. Hence, any effect of TSH on neurons could be ruled out.

Hence, the present study highlights the effect of altered hormonal profile (estradiol, prolactin and AMH) in patients of POS on the neuronal activity by increasing their excitability and lowering their reaction time.

LIMITATION

The present study came across a wide variation in the serum estradiol levels with the range of (2 pg/mL-3000 pg/mL), which resulted in the skewed data and hence we calculated the mode for serum estradiol rather than the mean, which showed us wide fluctuations in the serum estradiol levels.

CONCLUSION

The neuronal activity is slightly increased in the patients with Polycystic Ovarian disease which is quite evident due to decreased reaction time.

This increased neuronal activity could be attributed to hyperestrogenemia which acts through ERα receptors and is a documented neuroexcitatory hormone along with the stimulation of Tubero infundibular neurons in hypothalamus due to hyperprolactinemia resulting in increased dopamine levels in these patients, further adding to neuro-modulatory effect of oestrogen.

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PARTICULARS OF CONTRIBUTORS:
1. Student, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
2. Professor and Head, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
3. Consultant, Department of Geetanjali Fertility Centre, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
4. Student, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Manjinder Kaur,
Professor and Head, Department of Physiology, Geetanjali Medical College and Hospital, Udaipur-313002, Rajasthan, India.
E-mail: drmanjinder@yahoo.com

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