Press release - Abstract 1394: Alterations in clock genes expression in Eutopic and Ectopic Endometrial Tissue

EMBARGOED UNTIL SUNDAY 23 MAY 2021 AT 19:00 CET

New research suggests that night shift work is linked to menstrual irregularity and increased chance of developing endometriosis

According to a study being presented at the 23rd European Congress of Endocrinology (e-ECE 2021), on Sunday 23 May at 19:00 CET (www.ece2021.org), women working night shifts may be at a greater risk of menstrual irregularity and developing endometriosis. The research found a reduction in the expression of PER-2, CRY-1 and CLOCK genes along with an increase in REV-ERBb in ectopic compared to eutopic tissues. Prior to this research, there had been no previously published studies relating to the alterations in core clock-genes and the impact on women with endometriosis.

Endometriosis is a condition where tissue similar to the lining of the womb starts to grow in other places such as ovaries and fallopian tubes.[1] Endometriosis affects roughly 10% (190 million) of reproductive age women and girls globally.[2] The symptoms of endometriosis can vary - some women are badly affected, while others might not have any noticeable symptoms. In severe cases, it can be very painful and can cause infertility, miscarriages and ectopic pregnancies due to the probable effects of endometriosis on the pelvic cavity, ovaries, fallopian tubes, or uterus.[2] Disruption of circadian rhythm in night shift workers has been associated with menstrual irregularity, as well as an increased chance of developing endometriosis and ovarian tumours.

Dr. Narjes Nasiri-Ansari, Dr. Aggeliki Karapanagioti, and a team of colleagues under the guidance and supervision of Professor Eva Kassi from the National and Kapodistrian University of Athens, Greece, investigated the expression of the core clock related genes in paired eutopic and ectopic endometrial tissues. The study looked at 27 patients with confirmed ovarian endometriosis. Eleven (11) paired samples were collected from ovarian cysts (ectopic endometrial tissues) and normal endometrium (eutopic tissues), while further eight (8) ectopic and eight (8) eutopic endometrial tissues were collected from 16 different patients with the same diagnosis.

“The clinical evidence that circadian rhythm disruptions can be associated with endometriosis, is now confirmed at tissue level, by the altered expression of local clock genes in ectopic endometrium. Understanding the causes and effects of endometriosis will improve our ability to detect, manage or even prevent the condition. These findings provide us with a better understanding of biological rhythm disturbances,” commented Professor Eva Kassi.

The results from this study demonstrate an altered expression of CLOCK, CRY1, PER-2 and Rev-ERBb in normal endometrium tissues, as compared to ectopic endometrial tissues, indicating a disturbance of biological timing. However, the causal relationship of the altered expression pattern of these genes with the development of endometriosis needs further investigation.

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[1] NHS, Endometriosis. 2019. Accessed here: https://www.nhs.uk/conditions/endometriosis/
[2] World Health Organization, Endometriosis. 2021. Accessed here: https://www.who.int/news-room/fact-sheets/detail/endometriosis

Notes for Editors

1. The presentation "Alterations in Clock genes expression in Eutopic and Ectopic Endometrial Tissue" will be presented on Sunday 23 May at 19 CET.
2. e- ECE 2021 is held online on the 22-26 May 2021. You can access here.
3. The European Society of Endocrinology was created to promote research, education and clinical practice in endocrinology by the organisation of conferences, training courses and publications, by raising public awareness, liaison with national and international legislators and by any other appropriate means.

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Abstract
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Alterations in clock genes expression in Eutopic and Ectopic Endometrial Tissue

Category: Female reproduction

Introduction: Endometriosis is a dysplastic disease affecting approximately 7-10% of reproductive– aged women. It is defined as the presence of endometrial-like tissue outside the uterine cavity. Disruption of circadian rhythm in night shift worker has been associated with menstrual irregularity and increased chance of developing endometriosis and ovarian tumors.

The central circadian clock system located in hypothalamic suprachiasmatic nucleus (SCN) along with the peripheral clock system located in the reproductive tissues (endometrium) control the timing and length of the ovulatory cycle by regulating the expression of various hormones (i.e. gonadotropins, estradiol) which in turn regulate the expression of clock related genes and vise-versa.

To best of our knowledge, no studies related to the alterations in expression profile of the core clock-genes in human endometriosis have been published to date.

Aim: Herein, we aimed to investigate the expression of the core clock related genes in paired eutopic and ectopic endometrial tissues.

Methods: 27 patients with confirmed ovarian endometriosis were included in this study. 11 paired samples were collected from ovarian cysts (ectopic endometrial tissues) and normal endometrium (eutopic tissues) while further 8 ectopic and 8 eutopic endometrial tissues were collected from 16 different patients with the same diagnosis. The mRNA expression of Clock-genes (CLOCK, BMAL1,CRY-1, PER-2, ROR-α and REV-ERBb) was evaluated by qPCR in ectopic tissues and was compared with the eutopic tissues.

Results: The mRNA expression of PER-2 and CRY-1 genes was decreased in the total of ectopic tissues (n=19) compared to the total eutopic tissues (n=19) (p=0.02,p=0.02 respectively). A marginal reduction in the expression of CLOCK along with a marginal increase in REV-ERBb expression was noted (p=0.06 and p=0.09 respectively) in ectopic (n=19) compared to eutopic tissues (n=19).

The mRNA expression of clock-genes in the ectopic (n=11) compared to their paired eutopic tissues (n=11) revealed that the expression of PER-2 and CRY-1 genes were significantly lower(p=0.04,p=0.04, respectively), whereas REV-ERBb levels was significantly elevated (p=0.02). Additionally, a marginal decrease in the expression of clock gene in ectopic as compared to paired eutopic tissues was observed (p=0.09).

Of note, the mRNA levels of BMAL1 and ROR-α were not altered between our studied groups.

Conclusions: Our study demonstrates for the first time an altered expression of CLOCK,CRY1,PER-2,and Rev-ERBb in eutopic as compared to ectopic endometrial tissues indicating circadian clock disruption. However, the causal relationship of the altered expression pattern of these genes with the development of endometriosis needs further investigation.