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CASE REPORT

# GENETIC COUNSELING IN A CASE OF DELAYED SLEEP – PHASE

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## Summary

**As we gain more knowledge on genetic mechanisms, the demand for genetic consultations will increase, more areas of human illnesses becoming prone to such a medical activity. Hence genetic counseling was asked by a woman in case of a sleep disorder affecting three generations of her family. In the absence of specific gene tests for circadian rhythm disorders and during a genetic consultation consisting of a singular session, counseling the proband implied explaining briefly and up-to-date, the role of Clock-genes in defining a person's sleeping pattern, the yet blurred borderline between the influence of the environment and that of the inherited genotype, and also indicating behavioral techniques for managing the sleep deficiency.**
**Key words: genetic counseling, sleep disorder, delayed sleep – phase, semi-dominant inheritance pattern**

## Résumé

***Le conseil génétique dans un cas de retardement de la phase du sommeil***

**Au fur et à mesure qu'on connaît plus profondément le mécanisme de la génétique, la demande des consultations génétiques augmente et plus de domaines des maladies humaines deviennent enclins à ce type d'activité médicale. Ainsi une femme a demandé une consultation génétique dans le cas de trouble du sommeil qui a affecté trois générations de sa famille. A cause du manque de tests géniques au cas de la perturbation du rythme circadien, pendant une séance de thérapie, la conciliation du proband a consisté à lui expliquer brièvement, mais d'une façon mise à jour, le rôle des gènes Clock dans la définition du modèle du sommeil d'une personne, à lui éclaircir la frontière encore floue entre l'influence de l'environnement et du génotype hérité et à lui recommander des techniques comportementales nécessaires à la gestion du trouble du sommeil.**
**Mots clés: la thérapie génétique, le trouble du sommeil, le retard de la phase du sommeil, hérédité semi-dominante**

## Introduction

Sleep-wake cycles are one of the several influences of circadian rhythms in the human body. During the last decades researches have shown that circadian rhythms are a result of gene – environment interactions. (1, 2, 3) On model organisms it was shown that genes mainly involved in maintaining biological clocks in a normal range to control and synchronize the body's physiological processes are inherited in a semi-dominant (or incomplete) manner, because heterozygotes express an intermediate phenotype, somewhere in between that of the mutant homozygote and that of the normal homozygote. In 1985 Ralph Martin and Michael Menaker identified at a Syrian hamster (Mesocricetusauratus) in F2 the 1:2:1 ratio, meaning that 3 different circadian rhythms were present in the animals: of 20 hours, of 22 hours and of 24 hours. Despite the 1:2:1 ratio that is also present in case of codominant traits, this time the heterozygote did not show both traits (the dominant and the recessive one), but just an intermediate, having a circadian rhythm of 22 hours that is characteristic for the semi-dominant (or incomplete) inheritance pattern. (3)

### *Objectives*

This paper comes to emphasize the need of widening the medical fields in which genetic counseling could contribute to prevent psychological discomfort. Another aim of this study is to connect discoveries in the field of chronobiology to medical practice, respectively genetic counseling.

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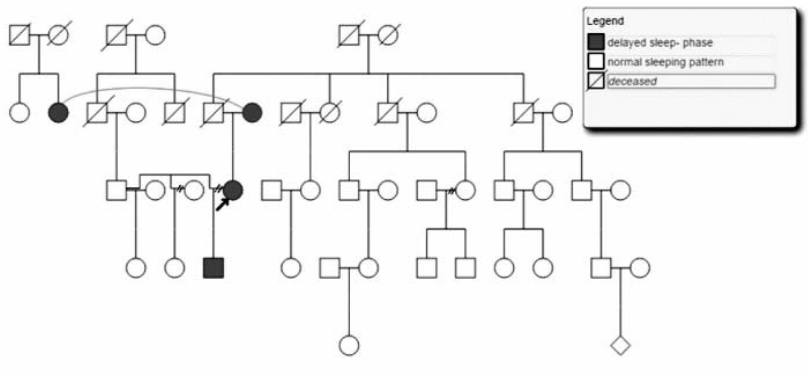


*Figure 1 - Family pedigree consistent with the autosomal dominant inheritance. The proband's maternal aunt has a normal sleeping pattern as detailed on the left.Pedigree drawn with PedigreeDraw*

## Case Presentation and Discussion

*In 2013 a 50 year old woman who complained of a life-long sleep disorder asked for a genetic consultation. She regularly went to bed late at night or even early in the morning and then she was sleepy during the next day. Her 20 year old son and her 77 year old mother had the same abnormal sleeping features. No other member of the family had the abnormal sleeping pattern as was shown by the pedigree method (fig. 1). The counselee came to the Policlinic No. 1 by her own choice for finding out if her sleep disturbance was an inherited trait. When being asked to come a second time for genetic counseling she refused, so that the two usual moments of a genetic consultation had to be resumed to that singular encounter.*

*From the discussion with the counselee the phenotype proved to be an overlap between the delayed sleep phase disorder type and the free-running type, as it is sometimes present in people who have the features of these circadian rhythm disorders(4), because their sleeping time becomes sometimes delayed progressively, one day after another.*

*In the case of semi-dominant transmitted traits it is difficult to make a clinical difference by examining the phenotypes of the heterozygote and the mutant dominant homozygote. This is why such traits are usually considered as autosomal dominant in medical genetics. In fact in this case the pedigree analysis alone confirmed the fact that the proband as well as her son were heterozygotes, because their fathers had a normal sleeping pattern. Still, for making a precise statement about the genotype, a targeted DNA analysis would be the only plausible, undeniable investigation, but there are no clock-genes in humans currently analyzed in medical practice, although the molecular feed-back loops that govern the wake – sleep rhythms were extensively researched (5, 6). In this situation the pedigree – as the only genetic investigation available during the genetic consultation - proved consistent with the autosomal dominant inheritance.*

*In the absence of any hormonal analysis or specialized sleep pattern investigation (like recording: body temperature, intensity of activity during the day and precise moment of falling asleep)the only diagnosis possible was that a sleep disorder was segregating in the family. From the description of the disturbance and the analysis of its presence in the family history there could not be made a doubtless difference between the delayed sleep phase syndrome and the free-running type. (7, 8)*

*The 50% recurrence risk of inheritance for future generations in case of autosomal dominant traits was explained to the patient and emotional support mixed with information on fundamental genetic knowledge dissipated some of the guilt feeling that had driven her to the consultation. She was also advised how by simple sleep hygiene methods (like darkness in the room while sleeping, following a certain diet, less activity in front of a computer screen before going to bed, etc.) she could try to create a sleep-wake pattern that would allow a better adaptation to social life and working environment.*

## Conclusions

Genetic counseling can be performed during a single session consultation using the information obtained from the family history. Patients can understand the mechanisms of their troubling symptoms and the inheritance patterns involved and thus overcome the emotionally difficult moments, when struggling to adapt their waking time to participate in morning scheduled obligations. With genetic information widely spread, demands for such specialized consultations might increase, while patients could benefit understanding more about their illness, its prevention, management, present research and learn how to deal with their feelings towards its presence not only in their own life but also in that of other family members.

***Conflict of interest:*** None

## References

1. Franken P, Thomason R, Heller HC, O'Hara BF. A non-circadian role for clock-genes in sleep homeostasis: a strain comparison.BMC Neurosci. 2007. 18;8:87
2. Circadian Sleep Disorders Network. http://www.circadiansleepdisorders.org/defs.php
3. Lowrey PL, Takahashi JS.Genetics of Circadian Rhythms in Mammalian Model Organisms.Adv Genet. 2011; 74: 175–230.doi: 10.1016/B978-0-12-387690-4.00006-4
4. American Academy of Sleep Medicine.http://www.aasmnet.org /resources/factsheets/crsd.pdf
5. Okamura H, Miyake S, Sumi Y, Yamaguchi S, Yasui A, Muijtjens M, Hoeijmakers JH, van der Horst GT. Photic induction of mPer1 and mPer2 in cry-deficient mice lacking a biological clock. Science. 1999 Dec 24;286(5449):2531-4.
6. von Schantz M. Phenotypic effects of genetic variability in human clock genes on circadian and sleep parameters. J Genet. 2008 Dec;87(5):513-9.
7. Lack CL, Wright HR. Circadian Rhythm Disorders I, Phase-Advanced and Phase-Delayed Syndromes.In:Morin CM and Espie C,ed. The Oxford Handbook of Sleep and Sleep Disorders.Oxford University Press; 2012; 28: 597 – 625.
8. Micic G, De Bruyn A, Lovato N, Wright H, Gradisar M, Ferguson S, Burgess HJ, Lack L.The endogenous circadian temperature period length (tau) in delayed sleep phase disorder compared to good sleepers. J Sleep Res. 2013; 22 (6): 617–624