EXPERIMENTAL RESEARCHES

CHANGES IN THE PATTERN OF SLEEP DISTURBANCES IN HEALTHY SUBJECTS UNDER 21-DAY ANTI-ORTHOSTATIC HYPOKINESIA

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ABSTRACT

Background. *Antiorthostatic hypokinesia (ANOH) reproduces some of the effects of weightlessness on the human body and is used to study adaptation to space flight conditions. It is known that ANOH affects nighttime sleep, but there is no information in the literature on the sequence of occurrence of sleep disorders in ANOH.*
The aim. *To study the dynamics of subjective changes in assessing sleep quality under conditions of antiorthostatic hypokinesia.*
Materials and methods. *Six healthy male volunteers (age from 26 to 34 years) participated in the experiment with 21-day ANOH. They were on a medical bed with a body inclination angle relative to the horizon of –6° for 21 days. To assess sleep quality, a structured questionnaire was used that assessed sleep duration, rate of falling asleep, night awakenings, the presence of daytime sleepiness, and daytime falling asleep.*
Results. *Based on the assessment of the dynamics of the sleep efficiency index (SEI), three stages of adaptation were identified. At the stage of acute adaptation (the first 3 days), there is a decrease in SEI from 96.4 to 91.3 ($p < 0.01$), a statistically significant prolongation of falling asleep from 17.6 to 33.6 minutes ($p < 0.01$), an increase duration of night awakenings up to 17.4 minutes, increase in daytime sleepiness by 11 %. In the next 3 days (the "recovery" stage), there is a statistically significant increase in SEI compared to the first stage to 94.7 ($p < 0.01$), but it remains statistically significantly lower than the background values ($p < 0.004$). The number of complaints about daytime sleepiness increases (up to 42 %), evening lights off term shifts later by 26 minutes. At the third stage (the remaining nights) there is a relative stabilization of the sleep-wake cycle.*
Conclusion. *Under conditions of 21-day ANOH, a gradual change in the pattern of sleep disturbances occurs. The most negative changes in terms of subjective assessment were noted in the first three days. Then there is an improvement in falling asleep, a decrease in night awakenings, combined with an increase in daytime sleepiness and the formation of a schedule with later lights off.*

Key words: *antiorthostatic hypokinesia, sleep, space flight, sleep efficiency index*

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ИЗМЕНЕНИЕ ПАТТЕРНА НАРУШЕНИЙ СНА У ЗДОРОВЫХ ЛЮДЕЙ В УСЛОВИЯХ 21-СУТОЧНОЙ АНТИОРТОСТАТИЧЕСКОЙ ГИПОКИНЕЗИИ

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РЕЗЮМЕ

Обоснование*.* *Антиортостатическая гипокинезия (АНОГ) воспроизводит некоторые эффекты воздействия невесомости на организм человека и применяется для изучения адаптации к условиям космического полёта. Известно, что АНОГ влияет на ночной сон, но в литературе отсутствуют сведения о последовательности возникновения нарушений сна при АНОГ.*

Цель работы. *Изучение динамики субъективных изменений оценки качества сна в условиях антиортостатической гипокинезии.*

Материалы и методы. *В эксперименте с 21-суточной АНОГ участвовали 6 здоровых мужчин-добровольцев (возраст от 26 до 34 лет). Они находились на медицинской кровати с углом наклона тела относительно горизонта –6° в течение 21 суток. Для оценки качества сна был использован структурированный опросник, оценивающий продолжительность сна, скорость засыпания, ночные пробуждения, наличие дневной сонливости, дневных засыпаний.*

Результаты. *На основании оценки динамики индекса эффективности сна (ИЭС) было выделено 3 этапа адаптации. На этапе острой адаптации (первые 3 суток) происходит снижение ИЭС с 96,4 до 91,3 ($p < 0,01$), статистически значимое удлинение засыпания с 17,6 до 33,6 мин ($p < 0,01$), увеличение продолжительности ночных пробуждений до 17,4 мин, усиление дневной сонливости на 11 %. В следующие 3 суток («восстановительный» этап) отмечается статистически значимое увеличение ИЭС по сравнению с 1-м этапом до 94,7 ($p < 0,01$), но он остаётся статистически значимо ниже фоновых значений ($p < 0,004$). Возрастает количество жалоб на дневную сонливость (до 42 %), сроки вечернего отбоя смещаются позже на 26 минут. На 3-м этапе (оставшиеся ночи) происходит относительная стабилизация цикла «сон – бодрствование».*

Заключение. *В условиях 21-суточной АНОГ происходит постепенное изменение паттерна нарушений сна. Наиболее негативные в плане субъективной оценки изменения отмечались в первые 3 дня. Затем отмечается улучшение засыпания, снижение ночных пробуждений в сочетании с увеличением дневной сонливости и формированием режима с более поздним отбоем.*

Ключевые слова: *антиортостатическая гипокинезия, сон, космический полёт, индекс эффективности сна*

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INTRODUCTION

Sleep has a role in supporting psychophysiological homeostasis at the proper level and plays an important role in the level of physical and mental performance [1]. Astronauts have reported sleep disturbances during spaceflight, which become less with the time spent in space [2].

The effect of spaceflight conditions that affect human sleep is also studied in ground-based modelling experiments. To be specific, head-down bed rest (HDBR) reproduces some of the effects caused by weightlessness on the human body and has been used to study adaptation to spaceflight conditions [3]. HDBR is an exposure that disrupts nighttime sleep. Staying for a long time with the head tilted downward reduces intracranial perfusion and leads to stasis in the jugular vein [4, 5], decreased systolic blood pressure and decreased heart rate [6], and increased intracranial pressure [7]. Body position also has an effect on liquor outflow and amyloid elimination activity [8]. It was previously shown with the use of polysomnography that under HDBR conditions there is a lengthening of the latent periods of stages 1, 2 and 3 of sleep, an increase in the duration of nocturnal awakenings and stage 2, as well as a decrease in the duration of stage 3 of sleep, the stage with rapid eye movements [9]. Studying sleep during the first day of hypokinesia has shown that there is a decrease in the stage 3 of sleep, the stage of sleep with rapid eye movements, an increase in stage 1, as well as a deterioration in the subjective quality of sleep [10, 11]. The other study observed a decrease in stage 4 sleep and an increase in the frequency of awakenings during experimental bed rest when the head was tilted downwards by –6° [12, 13].

In a single study, the authors have observed that during the first 3 days of HDBR, nocturnal sleep, level of daytime vigour and psychophysiological functions were not impaired, although a slight deterioration of attention function was observed in the morning [13].

In HDBR conditions, along with deterioration of sleep quality, daytime symptoms of circadian rhythm disturbance – the appearance of sleepiness, development of physical and mental fatigue are also observed [14].

An absence of any evidence in the literature about the consistency in the occurrence of sleep disturbances during HDBR determined the purpose of our work as a study of the dynamics of subjective changes in the assessment of sleep quality under conditions of head-down bed rest.

MATERIALS AND METHODS

The study is an open pre-experimental, prospective research. It was undertaken 5 days before HDBR (baseline assessment) and daily under HDBR conditions in the evening (for 21 days). Six practically healthy male volunteers aged 24 to 40 years (mean age – 29.8 ± 4.6 years) with body weight 75.2 ± 8.8 kg, body length 177.8 ± 5.3 cm, body mass index (BMI) 23.8 ± 2.7 kg/m^2 were enrolled in the study. All participants had undergone medical selection by the medical expert commission of the State Science Center of the Russian Federation – Institute of Bio-Medical Problems of the Russian Academy of Sciences, during which no diseases and pathologies preventing participation in the experiment were found. Each participant had signed a voluntary informed consent to participate in the experiment before being enrolled in the study. The study programme has been approved by the Biomedical Ethics Commission of the State Scientific Centre of the Russian Federation – Institute of Bio-Medical Problems of the Russian Academy of Sciences (SSC RF – IBMP RAS) (Protocol No. 621 dated August 8, 2022). The inclusion criteria for the study were the conclusion of the medical expert committee and consent to participate in the study.

The study was conducted on the basis of the SSC RF – IBMP RAS. Volunteers were kept in an anti-orthostatic position on a medical bed with a body angle relative to the horizon of –6°, without exercise and with moderate restriction of movement for 21 days.

Environmental factors: according to the study cyclogram, lights were turned off after 23:00. Additionally, the gadgets remained close to the participants at all times, but their use during the night was not monitored.

The study assessed data from questionnaires conducted 5 days before HDBR and daily under HDBR conditions in the evening (for 21 days). A structured questionnaire (non-validated) was specifically designed to identify sleep and wakefulness patterns, where participants answered questions related to sleep quality and sleep-wake cycle patterns in the evening. At its core were questions reflecting basic characteristics of sleep quality (sleep duration, rate of falling asleep, nocturnal awakenings) and wakefulness activity (presence of daytime sleepiness, daytime falling asleep, circadian distribution of activity). The questionnaire was not validated. The questionnaire is presented in Figure 1 (non-validated).

From the questionnaire data obtained, a sleep efficiency index (SEI) [1] was calculated as the ratio of the time from lights off term to final awakening to the same time minus the duration of falling asleep and nocturnal awakenings. The rest of the answers to the questions were scored. Responses reflecting worsening sleep and wakefulness quality corresponded to an increase in point estimates.

Statistical processing was performed using Statistica 10.0 program (StatSoft Inc., USA). In this analysis, the rank, quantitative (non-normal distribution) nonparametric Mann – Whitney test was used to compare unrelated groups.

RESULTS

A survey of trial participants revealed that 5 out of 6 healthy volunteers were bothered by long periods of falling asleep and night wakings during the first days of the experiment. Sleep disorders were associated by the participants with uncomfortable sleeping conditions and changes in the horizontal axis of the body, redistributing body fluids. In the following days at HDBR, their sleep problems became less of a problem.

Based on questionnaire results during the entire HDBR, all volunteers episodically reported difficulty falling asleep, nocturnal awakenings, increased daytime sleepiness accompanied by daytime sleepiness and drowsiness.

A study of sleep patterns based on a questionnaire we had designed revealed that during the 21-day HDBR period, the trial participants established a regime with a statistically significant later lights off and later morning awakening compared to background studies. The data are summarised in Table 1.

When the questionnaire has been analysed, it was found that under HDBR conditions, falling asleep for more than 30 minutes was observed to occur during 10 % of nights; in 24 % of cases, the time to fall asleep was between 15 and 30 minutes, and only 66 % of cases, the duration of falling asleep remained within the normal range (quick guide).

In analysing the number of awakenings within the HDBR condition, it was found that 10 % of the participants reported nocturnal awakenings lasting more than 30 minutes, and 90 % of the participants slept without prolonged awakenings.

Sleep
Sleep-related questions refer to past sleep.

1. What time did you go to bed?
2. How long did it take you to fall asleep?
   Up to 15 minutes
   Up to 30 minutes
   Up to 1 hour
   More than an hour
3. Waking up at night for more than 30 minutes
   0 times
   1 time
   2 times
   More than 2 times
4. What time did you finally wake up?

Wakefulness
Wakefulness questions refer to the past day.

1. Have you had any drowsy states or daytime naps?
   0 times
   1 time
   2 or more times
2. Have you had any daytime sleepiness?
   Yes
   No
3. Your activity during the day was higher
   Until 12:00.
   12 to 5:00 p.m.
   From 5:00 p.m.

FIG. 1.
Structured "Sleep – wake" questionnaire (non-validated)

TABLE 1

MAIN ANALYZED INDICATORS OF THE "SLEEP – WAKE" QUESTIONNAIRE

Indicators	Background data	HDBR data	*p*
Lights off (astronomical time)	23:35	00:47	0.001
Morning awakening (astronomical time)	07:25	07:52	0.01
Sleeping time (excluding falling asleep and waking time during night awakenings), h	7:08	7:15	0.90
Sleep efficiency index, %	96.43	94.39	0.26
Falling asleep time, h	0:29	0:40	0.37
Representation of drowsiness, %	33	63	0.044

An assessment of daytime wakefulness patterns revealed that throughout the HDBR, participants reported increased daytime sleepiness with occasional drowsiness. The presence of sleepiness and daytime falling asleep during wakefulness was noted in 61 % of cases, and in 8 % of cases daytime falling asleep could be more than 2 times per day.

SEI values, time to fall asleep, wakefulness time during nocturnal awakenings, and daytime sleepiness were used to assess sleep quality. The dynamics of these indicators is summarised in Figure 2.

The worst night was the first night of the HDBR stay. Compared to background data 5 days before HDBR, sleep on the first day was characterised by a decrease in SEI from 95 to 84 % ($p = 0.013$), a statistically significant prolongation of falling asleep from 17.55 to 42.1 min ($p = 0.050$), and an increase in the duration of nocturnal awakenings from 4.8 to 34.8 min.

Three stages of adaptive changes in the sleep-wake cycle in a 21-day HDBR condition were revealed based on visual assessment of SEI dynamics, time to fall asleep, duration of nocturnal awakenings, and daytime sleepiness.

Table 2 summarises the mean values of some indicators reflecting the quality of sleep and wakefulness for the highlighted stages.

Stage 1 – stage of acute adaptation, where during the first 3 days there is a decrease in SEI indices from 96.4 to 91.3 % ($p < 0.01$), statistically significant prolongation of falling asleep from 17.6 to 33.6 min ($p < 0.01$), increase in the duration of nocturnal awakenings up to 17.4 min; there is no increase in daytime sleepiness.

Stage 2 – recovery stage (next 3 days), where SEI statistically significantly increased compared to stage 1 up to 94.7 % ($p < 0.01$) but remained statistically significantly less than it was in the background ($p < 0.004$). The number of cases of daytime sleepiness indices increases by 38 %, the evening lights off time becomes even later by 26 min.

Stage 3 – the stage of relative stabilisation of the sleep-wake cycle (remaining nights). It is observed here the latest time of lights off – at 1 a.m. ($p < 0.003$) – in comparison with all stages of adaptation and background indicators (lights off time in the background – 23:36, in stage 1 – 23:54, in stage 2 – 00:20); the latest awakening time was at 8 a.m. (08:03) (in the background – 07:16, in stage 1 – 07:34, in stage 2 – 07:31), while sleep quality indicators (falling asleep time, night awakenings, SEI) and daytime sleepiness did not differ compared to background.

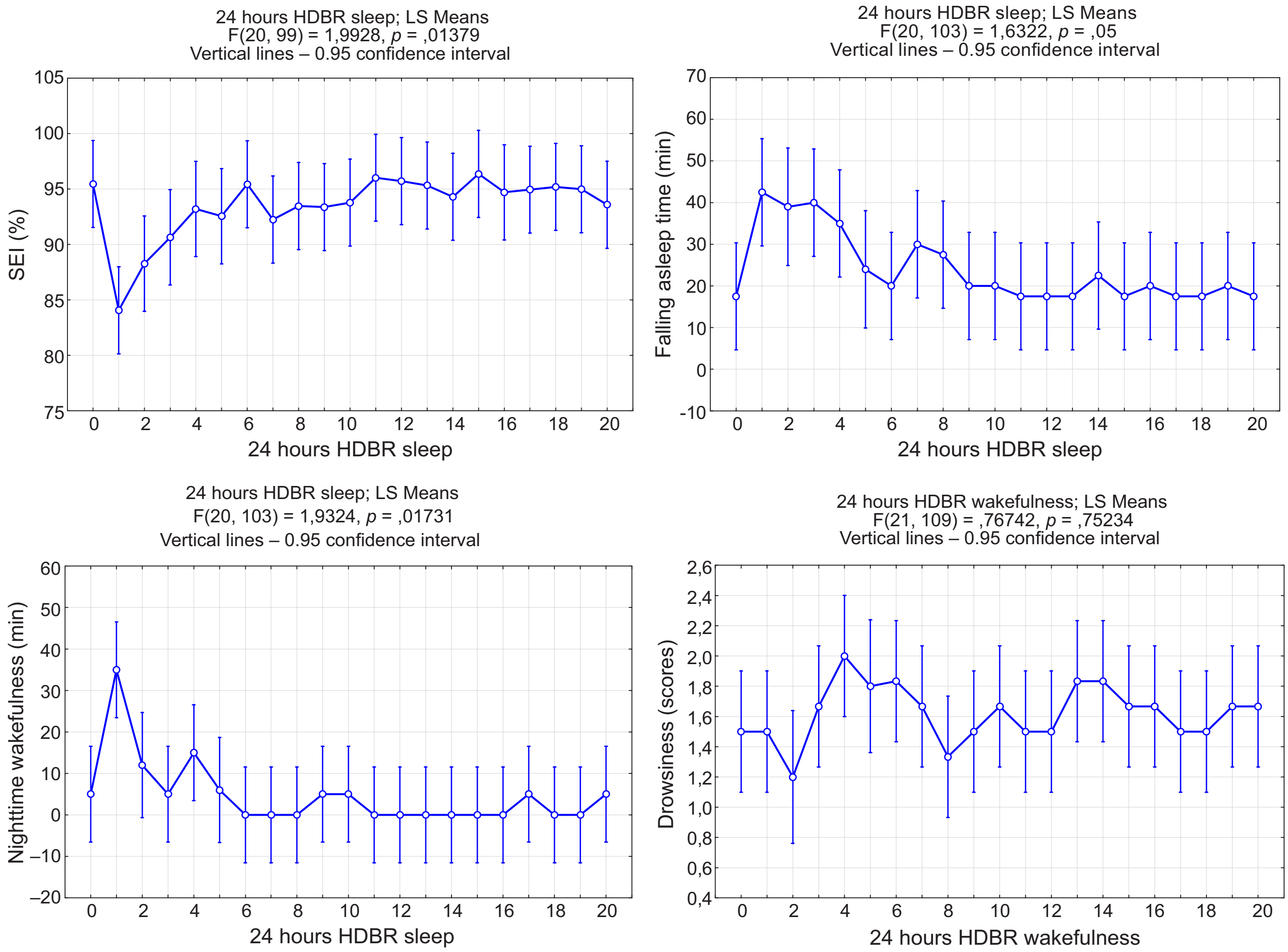

FIG. 2.

Changes in sleep and wakefulness characteristics under 21-day HDBR conditions

TABLE 2

STATE OF "SLEEP – WAKE" CYCLE INDICATORS AT DIFFERENT STAGES OF ADAPTATION ACCORDING TO QUESTIONNAIRE RESULTS

HDBR stages	Background	1st stage	2nd stage	3st stage
Lights off (astronomical time)	23:36	23:54	00:20	01:00
Falling asleep time, min	17.55	33.6	24.6	19.8
Wakefulness time during awakenings, min	4.8	17.4	6.9	0.09
Lights On (astronomical time)	07:16	07:34	07:31	08:03
Time in bed, h	7.63	7.66	7.15	7.04
Presentation of drowsiness, % of cases	33	44	82	62
SEI, %	96.33	91.32	94.73	94.91

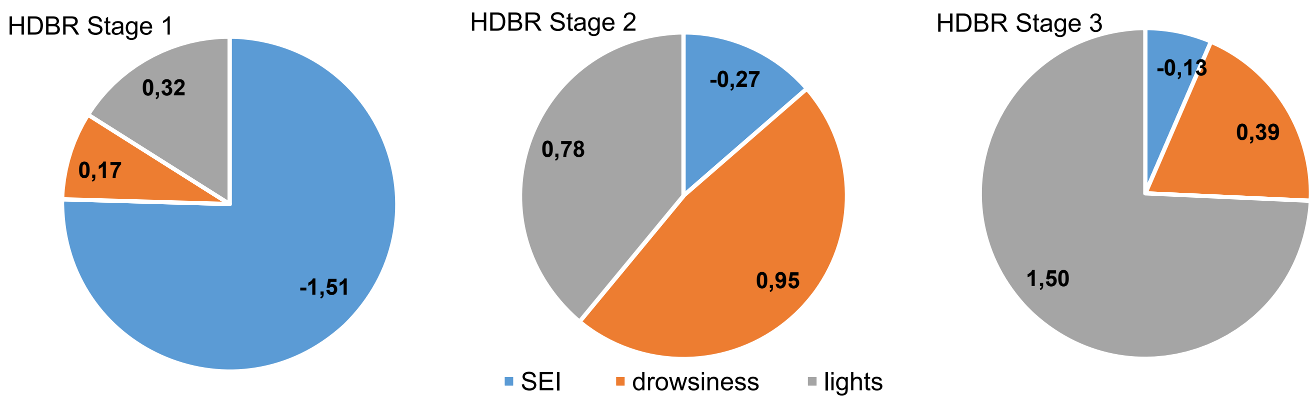

FIG. 3.

Differences of sleep-wake cycle indicators with background in standardised units at different stages of HDBR

Since the indicators are multi-dimensional, a data standardisation procedure was undertaken where the sample mean of the indicator is assumed to be 0 and its standard deviation is assumed to be 1. Differences with background values for all selected HDBR stages were calculated from standardised data. The results are summarised in Figure 3. The presented figure shows that in the acute period of adaptation the greatest changes are associated with a decrease in the sleep efficiency index, in stage 2 – with a shift in lights off time and an increase in daytime sleepiness, in stage 3 – with a shift in lights off time to later.

DISCUSSION

The interest in studying the particularities and timing of adaptation of somnogenic mechanisms to existence in extreme conditions is of definite importance, being able to predict the features of sleep in different periods of adaptation [2]. The results obtained allowed this study to identify successive stages of circadian system adaptation to HDBR conditions. The selected stages and their timing are conditional, as this selection was made on the basis of visual assessment of some indicators of the questionnaire describing the peculiarities of the sleep-wake cycle. Statistically significant differences have been revealed between these stages, but it is not entirely certain that the adaptation time stages that were defined are definitive, and further studies may present the time required for habituation to HDBR conditions in a different way. There is sufficient variation in SEI indices even during the period of acute adaptation (during the first 3 nights). Whereas on the first, worst night, SEI values are only 84 % (normal SEI should be more than 85 %), the following two nights the quality of sleep begins to recover – the average SEI value is 92 %. For this reason, it is possible that the acute adaptation phase may comprise only a single night and the remaining days may be classified as the sub-acute recovery phase.

Assessment of the state of the sleep-wake cycle at stage 2 of adaptation (recovery stage) and analysis of its clinical manifestations is an important component of the performed study. The gradual improvement in sleep quality during the recovery phase was combined with an unexpected finding of a 38 % increase in episodes of daytime sleepiness. The diagnosis of insomnia in clinical medicine is based not only on the assessment of sleep quality, but also on the assessment of wakefulness quality, including daytime sleepiness, as a characteristic indicating the negative impact of poor sleep quality on subsequent wakefulness [15]. This raises the suggestion that the increase in daytime sleepiness with improved sleep quality and unchanged sleep duration is a characteristic independent of sleep quality but possibly reflects an increased need for nocturnal sleep on days 4–6.

The remaining nights associated with stage 3 of relative adaptation were closest to background values. The assessment of this stage showed that changes in the sleep-wake cycle consisted in approaching the background values of the parameters that were assessed, which is a positive sign of adaptation. The fact that there is a significant shift in lights off and morning rise and fall to later hours during the relative stabilisation phase appears to be of particular interest. A shift to later bedtime is often revealed in healthy individuals under different stressful situations [16, 17]. It is assumed that the most likely reason for the development of later lights off time is probably caused by features of prior wakefulness (low physical activity). Ultimately, shifting the lights off time results in a later rise. The phenomenon of regime shift to later dates appears to be an important factor posing a potential threat to circadian rhythm stability in general [18].

Apart from the findings that were highlighted about the stages of adaptation, a number of shortcomings of the study have also been revealed, which impose a number of limitations. These include the small size of the group and the use of subjective assessments of the quality of the sleep-wake cycle.

CONCLUSION

Under HDBR conditions, there is a sequential occurrence of various circadian rhythm disorders: a decrease in sleep efficiency index as a result of lengthening of falling asleep and the appearance of nocturnal awakenings, followed by the development of hypersomniac symptoms (daytime sleepiness) against the background of improved nocturnal sleep, and then a gradual shift of the sleep regime to later periods. At different stages of circadian rhythm adaptation to HDBR conditions, the holistic picture of insomniac disorders changes, constituting a pattern of sleep disorders specific for each stage in healthy people under conditions of 21-day head-down bed rest.

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Conflict of interest

The authors of this article declare no conflicts of interest.

Ethical review

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