

ORIGINAL ARTICLE

Impact of the odors of vanilla extract and breast milk on the frequency of apnea in preterm neonates

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Abstract

Aim: We developed this study using an experimental design to determine the impact of the odors of vanilla extract and breast milk on apnea frequency in preterm neonates.

Materials and methods: We obtained the study data from 42 preterm neonates (16 vanilla, 13 breast milk, 13 control group) who had been admitted to the Neonatal Intensive Care Unit of Istanbul University meeting the case selection criteria. All groups were monitored on the first day without any intervention. On the second and third days, breast milk was placed in the incubators of the babies in the breast milk group and the sterile gauze that was vanilla-impregnated was placed in the incubators of the babies in the vanilla group. On the fourth day, the babies were watched without any interference.

Results: On the second, third and fourth days of the study, we determined that apnea frequency in the vanilla group neonates was significantly lower ($P < .00$) as compared to the breast milk and control groups.

Conclusion: Using vanilla extract in neonates suffering from apnea to reduce its frequency is an effective method.

KEYWORDS

apnea, breast milk odor, preterm neonate, vanilla extract odor

1 | INTRODUCTION

Apnea is one of the most common problems encountered in neonatal intensive care units, especially among preterm neonates, and it affects 80% of neonates born before the 30th week of gestation (Marlier, Gaugler, & Messer, 2005). The incidence of apnea is inversely correlated with gestational age and birth weight. It is noted that apnea frequency in preterm neonates at gestational week (GW) 26–27 is 78%, that it is 75% at 28–29 weeks, 54% at 30–31 weeks, 14% at 32–33 weeks, and 7% at 34–35 weeks (Zhao, Gonzalez, & Mu, 2011).

Since apnea frequency is seen to increase the lower the gestational age, it is thought to be associated with the immaturity of respiratory control mechanisms (Zhao et al., 2011). It is known that in preterm neonates, immature neurologic and respiratory systems, reduced hypercapnia and hypoxic responses, and difficulties with central respiratory control lead to apnea, which in turn decreases cerebral blood flow velocity and oxygenation. This increases the risk of cerebral damage (Marlier et al., 2005). Since the 1970s, first-line treatment of apnea has been pharmacological treatment. In general, in this type of treatment, the powerful respiratory stimulants, the methylxanthines (theophylline and caffeine), are administered to increase the metabolic rate, reduce muscle fatigue, increase diaphragm contractions and produce similar effects, but they also have an impact on apneic neonates' respiration as a central stimulant

The study was carried out at Istanbul University Istanbul Medical Faculty.

(Samancı, 2008). Doxapram is used by itself to control cases of apnea that do not respond to the methylxanthines (Zhao et al., 2011). However, none of the mentioned drugs seem to be fully effective when administered alone or concomitantly. The drugs also have undesirable and common side effects. Mechanical ventilation, a method that is also commonly used in neonate cases of frequently recurring apnea, has also been known to produce the adverse effects of hyperactivity, alteration of sleep patterns, tachycardia, metabolic-gastrointestinal and urinary tract disorders (Marlier et al., 2005; Mutlu, 2007). There is therefore a need for more effective non-pharmacological treatment methods with minimal side effects (Marlier et al., 2005). It is noted that non-pharmacological methods of treating apnea include positioning, cutaneous stimulation and aromatherapy (Zhao et al., 2011).

Aromatherapy is a form of natural treatment that makes use of aromatic essential oils derived by various methods from the bark, leaves, flowers, fruit, seed stems, roots or other parts of plant life. Lavender-based sitz baths, almond oil, beeswax and similar aromatherapy oils are used to treat neonate diaper rash (Jones, Kassity, & Duncan, 2001). In many recent studies, use of odor in preterm babies has been investigated. The researchers have reported that, the newborns had acute sense of smell (Gomella, 2012). AN ever-increasing number of recent studies have reported the physiological changes during breathing of odors in both full-term and preterm babies (Marlier et al., 2005). For example, after a fall in breathing, the preterm babies who have received oral tactile stimulation with a lemon-flavored swab stick restored an appropriate respiratory rate (Garcia & White-Traut, 1993). It has been reported that vanillin, as an olfactory stimulant, leads to enhancement of the orbito-frontal blood flow, detectable via near-infrared spectroscopy in normal newborns (Bartocci et al., 2000). It is asserted that the odor of vanilla, which is one of these sweet smells, stimulates the olfactory nerve, regulates respiration (Marlier et al., 2005) and reduces apnea frequency and prevents bradycardia (Garcia & White-Traut, 1993; Lecanuet & Schoal, 1996). Another sweet smell for newborns is the smell of breast milk. Although the literature reveals that some effects of the smell of breast milk are reducing hospital stay-time, relaxation, increasing sucking motions, and causing early transition to oral feeding (Bingham, Abassi, & Sivieri, 2003; Doucet, Soussignan, Sagot, & Schaal, 2007; Nishitani et al., 2009; Yıldız, Arkan, Gözümlü, Taştekin, & Budancamanak, 2011), its effects on apnea are largely unknown.

2 | METHODS

2.1 | Study design and sample

We developed this study using an experimental design to determine the impact of the odors of vanilla extract and breast milk on apnea frequency in preterm neonates.

One study reports (Marlier et al., 2005) the finding that the odor of vanilla extract reduces apnea by 44%. A 40% reduction in apnea was targeted in the present study as well and the alpha margin of error was found to be 5% (level of reliability, 95%). The beta margin of error was accepted as 20% and power as 80% and therefore in the calculation of sample size, the required number for each group was found to be 10 infants (total of 30). Taking into consideration that there might be case losses, sample size was kept larger than that calculated. In forming the groups, we randomly and equally distributed the cases among three groups in the Random Assignment Applet-Assumption College (<http://www1.assumption.edu/users/avadum/applets/RandAssign/GroupGen.html>). Thus, 16 preterm neonates were included in each group, which were the breast milk group, the vanilla group and the control group. Two neonates in the breast milk group were not able to suckle, one neonate from the breast milk group and three neonates in the control group were connected to CPAP (continuous positive airway pressure), thus we excluded a total of six neonates from the study. Therefore, the sample consisted of 42 preterm neonates (vanilla = 16, breast milk = 13, control = 13). Power analysis was performed on the results obtained from the data gathered. The power of the test on the basis of 95% alpha reliability was found to be 99.5%.

Measurements were conducted on 42 preterm neonates in the neonatal intensive care unit at Istanbul University Istanbul Faculty of Medicine. Their gestational ages ranged from 28 to 35 weeks. All the infants were inside the incubator. Infants were treated for apnea with bradycardia (theophylline and caffeine). They were not connected to mechanical ventilation and did not receive oxygen via CPAP. Infants did not have intracranial hemorrhaging or any congenital anomaly. In accordance with ethical standards, parents were informed and had to give written consent.

2.2 | Instruments

2.2.1 | Information form

This consisted of a total of 16 multiple-choice and open-ended questions about the neonate's date of birth, gestational week, birth weight-height-head circumference, gender, method of delivery, feeding method, the ages and educational status of the parents. It was filled by the researcher who was taking care of the file.

2.2.2 | Observation form

The observation form prepared by the researcher was used to record the number of apnea episodes, heart rate, oxygen saturation, and respiratory rate of the neonate in the last

24 h. The data of the vanilla, breast milk and control groups were recorded separately in this form.

The nurses were informed verbally by the researcher about the purpose and method of the research and the considerable issues before the research.

2.3 | Procedure

We completed the information form (Figure 1).

We grouped the monitored preterm neonates using the method of randomization.

Observation and registration were carried out by both researchers and nurses.

On the first day (24 h), all of the infants were watched with no intervention attempted and the observation findings were recorded.

On the second and third days of observation, we applied vanilla extract to the vanilla group and breast milk odor to

the breast milk group; a piece of sterile gauze soaked with vanilla essence and another piece of sterile gauze soaked with mother's milk were placed in the incubator. Vanilla extract was supplied from a herbalist. We used the original breast milk odor for the breast milk group. There was no intervention in the control group.

There were five neonates who were not receiving breast milk. Other infants were fed with breast milk exclusively or with both breast milk and formula. The infants who were not receiving breast milk were in the control or vanilla groups.

We applied approximately 15 drops of vanilla extract or breast milk to wet a sterile gauze pad and placed the pad inside the incubator, this amount was based on the findings of researchers who reported that 15 drops of vanilla would produce the best results (Marlier et al., 2005). Researchers also described applying vanilla extract to the tip of the infant's pillow. Since pillows were not used in our unit, we estimated that the tip of a 40 × 60 cm pillow would be about

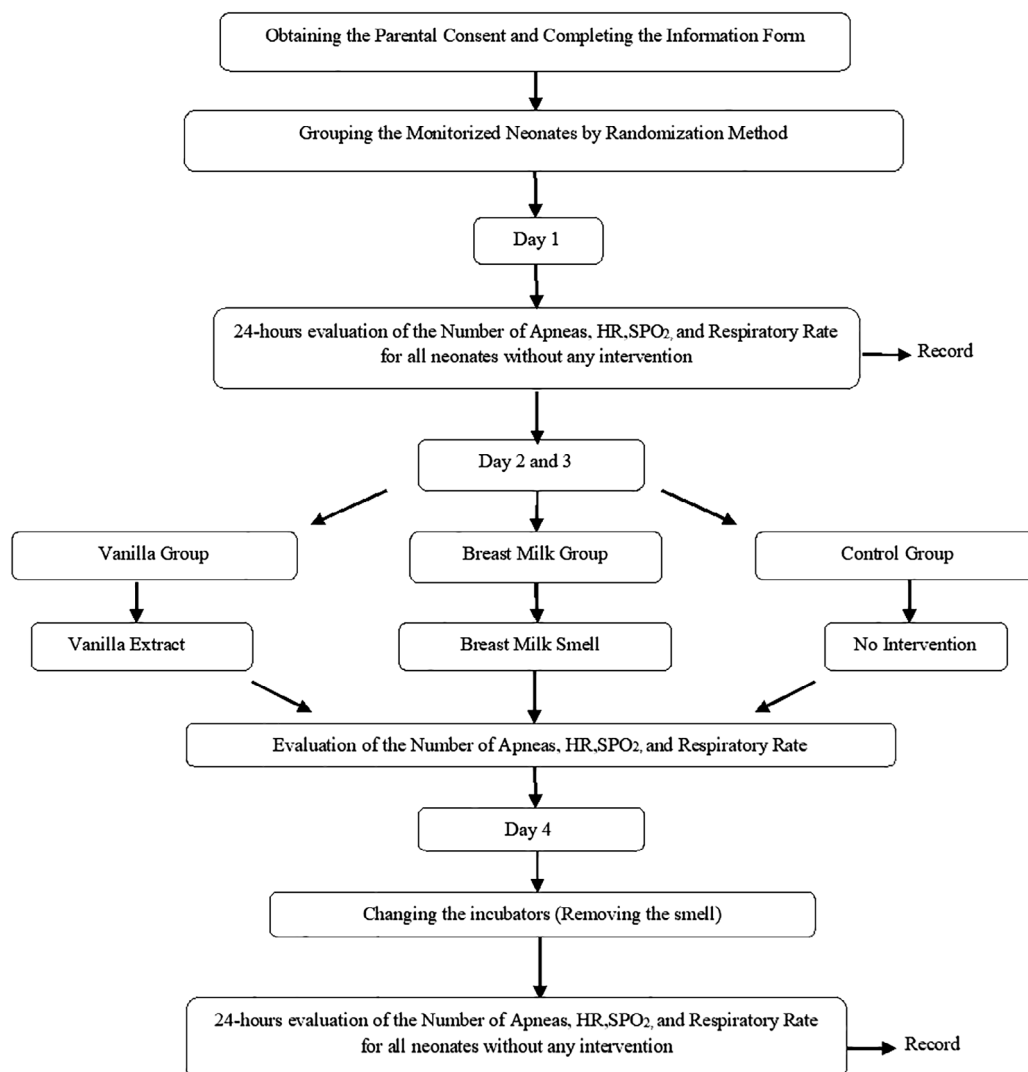


FIGURE 1 Study flow chart. HR, heart rate; SpO₂, oxygen saturation by pulse oximeter

15 cm away from the baby. We used the same measuring criteria for all neonates so they would be at the same distance from the odor.

The gauze pad was changed every 6 h to avoid milk spoilage and the risk of infection and at times that coincided with the nursing care hours of the unit.

All neonates were monitored over the course of the day for apnea episodes, heart rate, oxygen saturation and respiratory rate. The number of apnea episodes was recorded each time the infant had a bout of apnea in the 24 h. Since all of the monitors did not give averages of all 24 h values, other vital signs were obtained four times (09:00–15:00–21:00–03:00) a day, following the service routine. Then, the averages of the values were calculated and recorded on the observation form. The researcher used the data on the observation form.

On the fourth day, the babies were taken to another incubator to remove the breast milk and vanilla odor from the incubator. We later observed the infants again and followed up the groups in terms of the number of apnea episodes, heart rate, oxygen saturation and respiratory rate, and recorded the findings.

We made sure to adjust the temperature of the incubator to maintain the body temperature of the neonate at an optimal level.

2.4 | Data analysis

In the data analysis, we used our licensed SPSS (Statistical Package for Social Science) package for Windows 15. In the evaluation, we employed means, standard deviation, frequencies, percentiles, the Chi-square test and the two-factor repeated-measures analysis of variance. We evaluated the results within a 95% confidence interval at a significance of $P < .05$.

2.5 | Permissions and ethics

We obtained the written consent of the Istanbul University Istanbul Faculty of Medicine Ethical Committee. Consent was obtained from the parents of the neonates after they were informed about the study.

3 | RESULTS

When the descriptive characteristics of newborns in all groups were examined, differences between the groups were determined in terms of gestational week, postpartum age, birth weight, birth height and perinatal circumference. Most of the preterm newborns in the group were found to be girls, fed with breast milk and the feeding route was orogastric gavage. (Table 1).

When the mean values over the 4 days for the peak heart rate, oxygen saturation and respiratory rates of the preterm neonates in all groups were compared, we determined that

there was no statistically significant difference between the mean values of the preterm infants (Table 2).

The neonates in the control, breast milk and vanilla groups were compared in terms of mean values corresponding to the frequency of their apnea episodes using the two-factor repeated-measures analysis of variance. The results according to the time factor ($F = 5.349$, $P = .004$), according to the group characteristic ($P = .035$) and according to group-time interaction ($P = .000$) indicated significant differences.

When differences in terms of mean apnea frequency according to time (days) were compared separately within each group, no significant difference was found in the control or the breast milk group in terms of apnea episode frequency. However, a strikingly significant difference was found in the vanilla group. In further analysis, it was stated that the frequency of apnea attack in the vanilla group's babies showed a significant decrease in the second, third and fourth days compared to the first day. (Table 3).

When differences between apnea frequency means by groups were compared separately, on the first day, we found there was no difference between the groups in terms of apnea episode frequency. However, on the second, third and fourth days apnea episode frequency did display significant differences between the groups. The advanced analysis showed that on the second day, the apnea frequency rate in the vanilla group was lower than that in the breast milk group and the control group, and on the third day, apnea frequency in the vanilla group was again less than either the control or the breast milk group (Table 3).

4 | DISCUSSION

In our study, we aimed to observe the effects of odors on preterm neonates, and to achieve this, we monitored the peak heart rate, respiratory rate and oxygen saturation of the infants in the study over the course of 4 days. We found there were no significant differences between the infants in any of the groups in terms of peak heart rate, respiratory rate and oxygen saturation (Table 2). In our study, we found no significant differences ($P = .474$) between the neonates in terms of the frequency of apnea episodes in any of the groups on the first day; in other words, all of the groups displayed a similar number of apnea episodes. However, on the second ($P = .024$), third ($P = .014$) and fourth days ($P = .001$), there was a notable decrease in the apnea frequency in favor of the vanilla group and we determined this decrease to be statistically highly significant, especially on the fourth day (Table 3). The odor of breast milk was not found to have an effect on the frequency of apnea (Figure 2).

The study had some limitations. Since the study of (Marlier et al., 2005) was the only work available, the number of drops was based on the criteria used in this article.

TABLE 1 Descriptive characteristics and their comparison in preterm infants (N = 42)

Variable	Control group (n = 13)	Breast milk group (n = 13)	Vanilla group (n = 16)	F	P value
Gestational week, mean \pm SD	26.85 \pm 2.12	28.08 \pm 1.93	27.44 \pm 2.37	1.052	.715
Postnatal age (week), mean \pm SD	31.23 \pm 1.64	31.08 \pm 1.50	31.44 \pm 1.26	0.223	.243
Birth weight (g), mean \pm SD	872.92 \pm 245.70	948.08 \pm 199.07	982.50 \pm 306.21	0.659	.357
Birth height (cm), mean \pm SD	33.92 \pm 3.12	34.92 \pm 2.40	34.56 \pm 3.58	0.345	.710
Head circumference at birth (cm), mean \pm SD	24.92 \pm 2.29	26.31 \pm 2.14	25.44 \pm 2.80	1.052	.359
Variable	n (%)	n (%)	n (%)	χ^2	P value
Gender					
Female	8 (61.5)	10 (76.9)	10 (62.5)	0.894	.639
Male	5 (38.5)	3 (23.1)	6 (37.5)		
Way of feeding					
Breast milk	8 (61.5)	12 (92.3)	12 (75.0)	4.059	.398
Formula milk	3 (23.1)	-	2 (12.5)		
Mixed	2 (15.4)	1 (7.7)	2 (12.5)		
Route of feeding					
Orogastric	13 (100.0)	13 (100.0)	16 (100.0)	NA	
Gavage (OGS)					

Abbreviations: M, mean; SD, standard deviation.

However, in new studies, the effect of vanilla essence on apnea frequency can be observed by dropping more or less vanilla essence. As the records were kept for 24 h, the life of the same baby was evaluated by different nurses. We applied

the vanilla extract on 16 preterm newborns for 48 h. A broader sample may be useful to confirm the full value of the therapeutic value of vanilla extract odor and to confirm whether the treatment is appropriate.

TABLE 2 Comparison of the preterm neonates in terms of peak heart rate, respiratory rate, oxygenation mean values (N = 42)

Characteristics	Day 1 mean \pm SD	Day 2 mean \pm SD	Day 3 mean \pm SD	Day 4 mean \pm SD	P ^a
Control group (n = 13)					
Heart peak rate (beats/min)	138.28 \pm 8.99	141.08 \pm 8.13	141.62 \pm 8.79	137.19 \pm 7.24	.114
Oxygen saturation (%)	93.92 \pm 2.30	94.25 \pm 1.95	93.71 \pm 2.59	93.67 \pm 3.23	.944
Respiratory rate (breaths/min)	65.04 \pm 5.23	66.69 \pm 6.78	67.00 \pm 9.61	65.69 \pm 8.04	.447
Breast Milk group (n = 13)					
Heart peak rate (beats/min)	138.62 \pm 9.68	141.88 \pm 11.53	140.46 \pm 11.11	134.31 \pm 8.38	.253
Oxygen saturation (%)	93.77 \pm 2.86	93.02 \pm 2.59	94.71 \pm 3.22	93.98 \pm 2.09	.377
Respiratory rate (breaths/min)	65.29 \pm 8.19	61.21 \pm 7.66	59.15 \pm 8.03	59.00 \pm 7.90	.042
Vanilla group (n = 16)					
Heart peak rate (beats/min)	142.36 \pm 10.25	147.59 \pm 7.31	144.91 \pm 8.24	142.19 \pm 10.50	.083
Oxygen saturation (%)	94.58 \pm 2.43	94.59 \pm 2.59	94.22 \pm 2.59	94.98 \pm 3.19	.377
Respiratory rate (breaths/min)	66.00 \pm 7.95	62.72 \pm 6.23	63.33 \pm 6.93	61.55 \pm 7.97	.092

^aOne-may analysis of variance.

TABLE 3 Comparison of the groups over the 4 days in terms of the frequency of apnea episodes ($N = 42$)

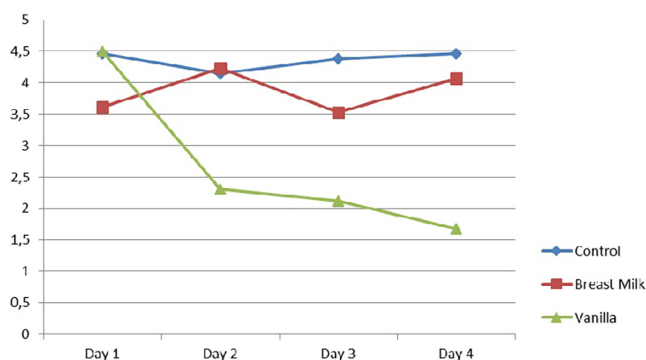
	Control ($n = 13$)	Breast milk ($n = 13$)	Vanilla ($n = 13$)	
Number of apneas/days (24 h)	$M \pm SD$	$M \pm SD$	$M \pm SD$	P^a
Day 1	4.46 ± 2.25	3.61 ± 1.71	4.5 ± 1.96	.474
Day 2	4.15 ± 2.23	4.23 ± 1.92	2.31 ± 2.18	.024*
				Breast milk group > vanilla group
Day 3	4.38 ± 2.25	3.53 ± 1.94	2.12 ± 1.89	.014*
				Control group > vanilla group
Day 4	4.46 ± 1.89	4.07 ± 1.80	1.68 ± 1.57	.001**
				Control group and breast milk group > vanilla group
p^b	0.587	0.693	0.000***	
(P:.001; 1d > 2d.3d.4d)				

^aKruskal-Wallis test. df: 2 (post hoc tests: Mann-Whitney U test with a Bonferroni correction).

^bFriedman analysis. df: 3 (post hoc tests: Wilcoxon test with a Bonferroni correction).

* $P < .05$; ** $P < .01$; *** $P < .001$; Abbreviations: M, mean; SD, standard deviation.

In many studies on the odor of breast milk, this odor is generally reported to have a pain-reducing effect (Nishitani et al., 2009; Goubet, Strasbough, & Chesney, 2007) while increasing sucking motions, facilitating oral feeding and providing relaxation (Bingham et al., 2003; Doucet et al., 2007; Yıldız et al., 2011) as well as increasing oxygenation and reducing troubled respiration (Rattaz, Goubet, & Bullinger, 2005). It has been shown that mean values for oxygen saturation in infants exposed to the odor of breast milk remain approximately the same but that only the respiratory rate decreases significantly, remaining stable on the last day. This suggests the odor of breast milk has an effect on the respiratory rate. We found no study in the literature on using the odor of breast milk to reduce the frequency of apnea. In our study, we hypothesized that the smell of breast milk would be stimulating and would be effective in apnea, but we found that it was in fact not effective in reducing the frequency of apnea episodes.

**FIGURE 2** Comparison of apnea frequency between groups for 4 days

However, the odor of vanilla extract has been reported to have an effect on apnea. Marlier et al. (2005) found in their study with 14 preterm neonates with apnea but without bradycardia, that exposing the infant to the smell of vanilla extract reduced their apnea and that this reduction was effective in all of the neonates. Edraki, Pourpoulad, Kargar, Pishva, and Zare (2013) reported the result of their study with 36 preterm infants, stating that the odor of vanilla extract was beneficial in treating apnea, and that vanilla was particularly effective because it stimulated the cerebral center of respiration as the odor traveled through the nasal mucosa. Apnea is a respiratory arrest in infants for 20 s or more and accompanied by hypoxia or bradycardia (Konak et al., 2014). The bradycardia is accompanied by an apnea that cannot be as much oxygenated as in the newborn. It is also asserted that the smell of vanilla extract increases the blood flow in the left orbito-frontal region, significantly increasing blood oxygenation (Bartocci et al., 2000). The bradycardia apnea case was more common in our neonatal intensive care unit. We thought that the odor of vanilla extract would prevent apnea by stimulating respiration and decreasing bradycardia. The results of this study confirm the positive effect of vanilla extract odor on the apnea. Drugs used in the pharmacological treatment of premature apnea decrease apnea by acting as a central stimulus of respiration. However, there are many negative side effects, while there is no known side effect of vanilla extract odor. The results of this study show that caffeine and doxapram therapy have a therapeutic effect in the treatment of cases where apnea frequency is not reduced, even though the treatment is taken.

In the present study, it was concluded that the odor of vanilla effectively reduced apnea frequency in preterm

neonates while the odor of breast milk had no such effect. This method, due to being simple, inexpensive, easy to implement, and effective, can be utilized for preterm neonates who have apnea with bradycardia.

DISCLOSURE

The authors have no financial relationships relevant to this article to disclose.


CONFLICT OF INTEREST

The authors have no conflicting interest to declare.

AUTHOR CONTRIBUTIONS

SB designed the study. BK collected the data. BK analyzed the data. BK, SB prepared the manuscript. We confirm that all listed authors meet the authorship criteria, and all authors are in agreement with the content of the manuscript.

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