High prevalence of lactase non-persistence among indigenous nomadic Nenets, north-west Russia

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Objectives. The frequency of adult-type hypolactasia (lactase non-persistence) varies widely among different ethnic groups. The cultural historical hypothesis assumes a link between the occurrence of hypolactasia and the distribution of dairy farming. The nomadic Nenets have been reindeer herders for generations and have therefore not consumed any dairy products. The hypotheses here was that the prevalence of lactase non-persistence (−13910 C/C genotype) among Nenets people having four Nenets grandparents is high, while the prevalence among Nenets originating from ethnically mixed families is lower.

Study design. The material was collected in four typical Nenets settlements in the Nenets Autonomous Okrug in Russia. One-third of the adult Nenets population were invited to answer a questionnaire and to donate buccal samples for genotyping by a doctor from the team of medical professionals who make rounds in this area. The total number of available participants was 177.

Methods. Genotyping was performed with the AbiPrism system. We used the method of concordance of grandparents’ national origin to ascribe ethnicity.

Results. The prevalence of adult-type hypolactasia (−13910 C/C) among Nenets who had four Nenets grandparents was found to be 90%. The figures among others reporting three, two and one grandparent of Nenets origin were 72, 60 and 28%, respectively.

Conclusion. The findings are in accord with the cultural historical hypothesis.

Keywords: adult-type hypolactasia; lactase non-persistence; cultural historical hypothesis; nomadic Nenets; genotyping.

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been performed previously. As the Nenets lifestyle has remained unchanged over the years, we tested the hypothesis that the prevalence of lactase non-persistence (−13910 C/C genotype) among Nenets people having four Nenets grandparents is high, while the prevalence among Nenets originating from ethnically mixed families is lower.

This study follows a series of investigations of Finno-Ugrian populations, the aim being to investigate the impact of ethnic background on the prevalence of adult-type hypolactasia among the Nenets.

Material and methods

The concept of ethnicity implies one or more of the following: shared origin or social background; shared culture or traditions which are distinctive, maintained between generations, and lead to a sense of identity and group; and a common language or religious tradition (23). The method of concordance of grandparents’ national origin to ascribe ethnicity was used in the present study. The term ethnicity is used in the biological sense.

Collection of material was made in four settlements of the Nenets Autonomous Okrug (NAO), Archangelsk Region, where the indigenous Nenets live (Fig. 1, (24)). The Nenets represent 15.2% of the whole population of the NAO, where other ethnicities including Komi and Russians are also settled (25).

The main occupations of the inhabitants of the four settlements are reindeer husbandry, hunting, fishing and also in one case cattle farming. These settlements are thus typical for Nenets living conditions and the sample here can be considered representative for the whole nomadic Nenets population. According to official information, the total number of adult Nenets in these settlements was 493. Of these 42.6% were male and 57.4% female aged from 19 to 80 years old (Table I).

Since there are no primary health care centres in many of the settlements in the NAO a team of medical professionals make rounds in this area. The GP from this team has an official list of Nenets obtained from the local administration. For the present study every third person was selected from this list and requested to answer a questionnaire and donate buccal samples for genotyping. If a selected person was absent from the settlement when the study was performed, the following person on the list was invited to participate. Men were absent more often than women. There were thus 181 participants for the final analysis.

Sample description

All selected subjects were informed of the aim of the study and gave written informed consent before participation and provided information on their ethnicity and place of birth as well as the ethnicity and place of birth of...
their parents and grandparents. Buccal samples for genotyping were taken from all 181 subjects. However, while all of them considered themselves Nenets, according to the grandparents’ ethnicity only 91 (50.3%) were accepted as native Nenets having all four of their grandparents of Nenets origin. Those with 1, 2 or 3 Nenets grandparents (90 in total) were also taken for comparison.

In the process of genotyping the buccal samples, four samples remained undetermined. Three of them were from females aged from 42 to 61 years old, and one was from a 33-year-old male of mixed ethnicity. Two of the females were of native Nenets origin, having four Nenets grandparents. Thus, 89 people of clear Nenets origin aged 19–80 years old (mean 45.8), of whom 91.0% were female and 9.0% male (Table I), were selected for the frequency analysis. The selection process is shown in Fig. 2.

The study was approved by the Health Care Department of the NAO and the Ethical Committee of the Northern State Medical University, Arkhangelsk, Russia.

Table I. Characteristics of the study population (n = 493) and participants (n = 177) by gender and age

| Gender       | All Nenets inhabitants of particular settlements | 4 Nenets grandparents | Less than 4 Nenets grandparents |
|--------------|-----------------------------------------------|-----------------------|--------------------------------|
|              | n     | %     | n     | %     | n     | %     |
| Gender       |       |       |       |       |       |       |
| Male         | 210   | 42.6  | 8     | 9     | 8     | 9     |
| Female       | 283   | 57.4  | 81    | 91    | 80    | 91    |
| Age distribution |       |       |       |       |       |       |
| 19–40        | 221   | 44.8  | 35    | 39    | 45    | 51    |
| 41–60        | 200   | 40.6  | 39    | 44    | 33    | 38    |
| 61–80        | 72    | 14.6  | 15    | 17    | 10    | 11    |
| Total        | 493   | 100   | 89    | 100   | 88    | 100   |
The study was conducted in accordance with the United Nations Declaration on the rights of indigenous peoples (26).

Genotyping
The buccal samples were genotyped in the Forensic Laboratory of the University of Tampere. The polymorphism of lactase persistence/non-persistence SNP rs4988235 was determined using the TaqMan Human Custom Genotyping Assay from Applied Biosystems. The assay was performed with the AbiPrism 7900 HT sequence detection system (Applied Biosystems, CA, USA) according to the instructions provided with the assay.

Statistical analysis
We used frequency and cross-tabulation analysis. Differences between groups were tested by $\chi^2$ test. Statistical analyses were performed with SPSS version 15.0 (SPSS Inc. Chicago, IL, USA).

Results
The prevalence of lactase non-persistence genotype ($-13910$ C/C) among Nenets having only Nenets in two previous generations was found to be 90% (Table II). The prevalence among others who regarded themselves as Nenets and reported three, two or one grandparent of Nenets origin was shown to be 72, 60 and 28%, respectively ($p < 0.0001$). Other grandparents were mostly Komi (10.7%) and Russians (8.8%), followed by Ukrainians, Byelorussians and others in single cases.

Discussion
The prevalence of adult-type hypolactasia ($-13910$ C/C genotype) among the nomadic Nenets inhabiting the Nenets Autonomous Okrug and having all parents and grandparents of Nenets origin was found to be as high as 90%, which is in accord with our hypothesis. The prevalence of the lactase non-persistent genotype among Nenets with three, two or one grandparent of Nenets origin was lower in comparison with those having all Nenets grandparents.
The four settlements in which the collection of material was made are typical for Nenets living conditions and can therefore be considered representative for the whole nomadic Nenets population. The distribution by gender in the study group differed from that in the overall population of the area. Compared to Nenets women, Nenets men were absent more often from the settlements due to reindeer keeping, fishing, hunting or for personal reasons. However, since gender does not affect the lactase persistent/non-persistent genotype, this fact caused no biases. The age of participants involves no bias in the genetic method and therefore has no effect on the results.

The findings here bring to light the actual prevalence of adult-type hypolactasia among the indigenous Nenets, since genotyping and the method of concordance of national origin (23) were used for the first time to investigate the frequency of the lactase persistence/non-persistence genotype among this group. Genetic testing is a highly sensitive and highly specific method of adult-type hypolactasia (lactase non-persistence) diagnostics (27) while the method of concordance of national origin allows definition of the ethnicity of investigated persons. We used the term ethnicity in the biological sense in our study. Since all participants were of active age and capable of understanding the questionnaire, we may rely on the accuracy of the answers. Nenets participants had no problems in defining the ethnicity of their grandparents. The Nenets are traditionally careful to preserve their ethnic features and are indubitably aware of family and relatives. Previously published data on lactose malabsorption among the Nenets have presented a sample of 9 persons of Nenets origin from Siberia (13). According to the lactose tolerance test, the prevalence was estimated at 78% (7 of 9 persons). Another study involving 108 Nenets from Siberia showed the prevalence of lactose malabsorption among them to be 88% (22). The prevalence of lactose malabsorption among the Nenets as determined by indirect methods was thus found to be high. Our present results amplify these previously published data and enhance their accuracy in that the genotyping has been confirmed to correlate closely with dissacharidase activity in the small intestine (27).

The impulse to discover differences in the prevalence of hypolactasia among indigenous peoples derives from the considerable variability in the frequency of lactase non-persistence among them. So far no population with 100% frequency of \(-13910\) C/C genotype has been discovered. Previously published data on the prevalence of lactose malabsorption among indigenous groups inhabiting different territories in the Russian Federation show the highest prevalence to obtain among the Khants (near the River Ob), with a figure of 94% (11). The frequency of the C/C-13910 genotype in Komi-Permyaks was found to be 42%, while the Chukchi have an 89% frequency of the lactase non-persistent genotype (22). Among other arctic populations a high prevalence of lactose intolerance in 70% investigated by lactose tolerance test was shown among northern Alaskan Eskimos (28). Such genetic differences in neighbouring populations can be explained by different earlier histories.

The Nenets have traditionally never consumed cow milk before the 20th century. Historians believe that this group (formerly Samoyeds) split apart from the Finno-Ugrian speaking group around 3000 BC, and then possibly mixed with the Turkic and Altaic-speaking group around 200 BC. Some groups settled in Siberia, while others remained nomadic and maintained reindeer herding and hunting, traveling long distances (7,29). Cattle breeding is reported to have started among the Nenets during the Soviet era, the first farms being organised in Nenets villages in the 1930s (8,10). The Nenets tribes have thus been isolated and more likely only during the last 70–80 years the gene flow from neighbouring populations has played a role in the prevalence of lactase non-persistence. Those who still have mostly Nenets forebears retain one of the highest prevalences of adult-type hypolactasia.

Our findings support and amplify the cultural historical hypothesis of hypolactasia. Not only the history of milk drinking but also the gene flow from other populations exerts an influence on the frequency of lactase non-persistence.

| Number of grandparents of Nenets origin | C/C-13910 |  | C/T-13910 or T/T-13910 |  | Total |  |
|---|---|---|---|---|---|---|
| 4 | 80 | 90 | 9 | 10 | 89 | 100 |
| 3 | 13 | 72 | 5 | 28 | 18 | 100 |
| 2 | 31 | 60 | 21 | 40 | 52 | 100 |
| 1 | 5 | 28 | 13 | 72 | 18 | 100 |
| Total | 129 | 73 | 48 | 27 | 177 | 100 |
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I declare that the authors have no competing interests which might be perceived to influence the results and/or discussion reported in this article.

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