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Fluctuating Asymmetry of Rodent Cranial Structures in an Industrial Pollution Gradient

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Abstract—Fluctuating asymmetry (FA) of the mandible shape has been analyzed in bank voles from the zones affected by pollution from three copper smelters in the Urals. It has been shown that there is the necessity for a detailed analysis of the material, since the level of FA may depend on population parameters. Regardless of the pollution level, FA of the mandible region including the lower part of the mandibular body, ramus and processes is higher than in the diastema region. A gradient effect of toxic exposure on FA has been revealed: an increase in its level under increasing technogenic impact is clearly manifested along local pollution gradients.

Keywords: fluctuating asymmetry, ontogenetic homeostasis, rodents, industrial pollution, cranial characters, bioindication

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Subtle, nondirectional deviations of bilaterally symmetrical characters from perfect symmetry, or fluctuating asymmetry (FA), are widely used as an indicator of stability of ontogenetic processes. This approach is based on the concept of ontogenetic homeostasis as the ability of an organism to follow a definite program of development under a certain set of conditions. Asymmetry in the development of a character whose formation on the right and left body sides is controlled by the same genotype and environmental conditions is a result of disturbance in ontogenetic processes (Van Valen, 1962; Zakharov, 1987; Palmer, 1994). Thus, FA reflects the degree of this disturbance, or, in other terms, developmental noise (Waddington, 1957), random spontaneous developmental variability (Astaurov, 1978), or developmental instability (Palmer, 1994). An increase in FA is usually attributed to the stressful effect of internal (genetic) or external (environmental) factors (Zakharov, 1987; Clarke, 1992; Parson, 1992; Palmer and Strobeck, 2003), and estimates of its level are widely used in fundamental and applied research.

FA is also used as a criterion of well-being of natural populations in assessing the consequences of industrial pollution of the environment. However, the results obtained with FA are not always unambiguous. Thus, studies of FA in craniological characters of rodents from regions polluted with petroleum products revealed both an increase in developmental instability (Veličković, 2004) and the absence of any significant effects (Owen and MacBee, 1990). The situation with studies on FA in areas around industrial facilities is similar: either increased developmental instability (Nunes et al., 2001) or, on the contrary, a significant decrease in FA of some craniometric characters (Gileva and Kosareva, 1994) have been reported.

We have studied FA of craniological characters in rodents exposed to different levels of technogenic impact using four species from two families (Gileva et al., 2007): the northern mole vole *Ellobius talpinus,* common vole *Microtus arvalis*, East European vole *M. rossiaemeridionalis* (Cricetidae), and house mouse *Mus musculus* (Muridae). It has been found that complex morphological structures such as the cranium and mandible do not always exhibit a distinct relationship between the level of developmental instability and technogenic stress, and provide different information on the nature of FA. Distinct interspecific differentiation corresponding to the taxonomic positions of the above species and the sequence of their evolutionary divergence has been observed in FA of the cranium. Apparently, the influence of factors related to species specificity of individual development plays no less important role than technogenic stress in determining the level of developmental instability in the cranium. In contrast, FA of the mandible in the four species has proved to be similar, suggesting that the role of evolutionary (taxonomic) signal in FA formation is insignificant in this case.

Our subsequent study FA of the mandible, performed using geometrical morphometry (Bookstein,

Table 1. Atmospheric emissions from the MUCS, KCSW, and KCS (data on heavy metals are shown in total for all forms of their pollutant compounds)

Emission source	In operation since	Year of measurement	Emissions, 1000 t			Including (t/year)			
			total	SO_2	dust	Cu	Zn	Pb	As
KCS	1910	1970[1]	370.0	364.5	28.8	1.53	4.55	2.57	1.92
		1990	50.7	46.9	3.8	0.44	1.36	0.25	0.08
		2005	41.0	38.1	1.3	0.34	–	0.02	0.01
KCSW	1914	1989[2]	95.3	85.5	6.9	0.41	0.26	0.51	0.17
		1993[2]	56.4	51.9	3.7	0.05	0.18	0.21	0.13
		2006[3]	23.1	20.9	–	–	–	–	–
MUCS	1940	1980	253.0	201.7	25.1	4.403	–	1.08[4]	0.94[4]
		1995	78.5	64.6	10.4	0.85	0.80	0.29	0.21
		2005	28.8	24.3	3.0	0.05	0.26	0.15	0.02

References: [1]Stepanov et al., 1992; [2]Vorobeichik et al., 2006; [3]*Gosudarstvennyi doklad...*, 2006; [4]Zyrin et al., 1986; other data from Kozlov et al., 2009.

1991) in line with the concept that the ontogeny of complex cranial structures has a modular pattern (Yalkovskaya et al., 2014), has revealed differences in FA values between the constituent parts (modules) of the mandible. Thus, the mandible of rodents is formally a paired bone consisting of right and left hemimandibles, but each hemimandible, in turn, consists of at least two modules: anterior (diastemal) and posterior, which includes the lower part of mandibular body, ramus and processes. Discrimination between these modules is valid not only in terms of their functioning and sequence of development of mandible but also in view of differences in the pattern of FA. A series of publications are available where the modular organization of the mandible is analyzed in the genetic, ontogenetic, and evolutionary contexts (Atchley and Hall, 1991; Leamy, 1993; Klingenberg et al., 2001, 2003). Far less attention has been devoted to the question concerning the prospects of this approach in monitoring research, including the assessment of the consequences of exposure to technogenic impact based on FA values.

The purpose of this study was to analyze FA of the shape of the mandible taking into account the modular pattern of its development in rodents from a gradient of industrial pollution using the example of bank voles (*Clethrionomys glareolus* Schreber, 1780) from the zones of impact from nonferrous metal works in the Urals.

MATERIAL AND METHODS

The study was performed in three model areas exposed to emissions from the Middle Ural Copper Smelter (MUCS), Kirovgrad Copper Smelting Works (KCSW, the Middle Urals), and Karabash Copper Smelter (KCS, the Southern Urals). The bank vole was chosen as a model because it is regarded as a background species and has been traditionally used in ecotoxicological monitoring performed in the study region (Vorobeichik et al., 2006; Mukhacheva and Bezel', 1995; Mukhacheva et al., 2010). The above copper smelters are the largest in the Urals and have been in operation for 75 (MUCS) to more than 100 years (KCSW and KCS), affecting the surrounding ecosystems. The structure of emissions from these plants is generally similar (Table 1): the main gaseous component is sulfur dioxide, inorganic dust is enriched in heavy metals with prevalence of copper (MUCS), lead (KCSW), or both these metals and arsenic (KCS). The amount of emissions has decreased significantly in the past decades, after modernization of production cycles, but the accumulated amounts of pollutants are still significant.

Based on analysis of heavy metal accumulation in natural media (soil, forest litter, and snow) and geobotanical relevés, stationary forest plots previously established at different distances from the polluters were used in this study as impact (1–2 km), buffer (4–6 km) and background plots (18–35 km) (Vorobeichik et al., 1994, 2006; Mukhacheva, 2007; Mukhacheva et al., 2010). The choice of these model plots in the gradient of technogenic load was also supported by data on the concentrations of four heavy metals (lead, cadmium, copper, and zinc) in the liver of bank voles from the same areas (Table 2).

Studies in the Southern Urals were performed in 2010; in the Middle Urals, in 2006. In addition, the material for analyzing FA from the impact plot near MUCS included voles trapped in 1990, and that from the background plot near KCSW, voles trapped in 2002, 2006, and 2008. As an external control, we also

Table 2. Concentrations of heavy metals in the liver of bank voles from three industrial pollution gradients in the Urals, μg/g dry weight

Emission source	Zone	*N*	Concentration, geometric mean (min–max)			
			Cu	Zn	Cd	Pb
KCS	Bg	101	13.08 (5.27–46.74)	98.99 (70.53–135.94)	1.26 (0.03–16.61)	1.30 (0.01–10.77)
	B	58	13.73 (8.77–39.79)	94.59 (78.31–153.92)	1.71 (0.07–16.58)	2.49 (0.03–10.18)
	I	56	10.62 (5.71–35.41)	86.54 (53.42–166.71)	1.89 (0.40–55.40)	2.86 (0.30–24.78)
KCSW	B	118	14.96 (3.23–25.45)	96.13 (52.84–211.68)	0.23 (0.02–9.03)	1.45 (0.37–22.26)
	I	14	14.06 (9.46–18.47)	89.71 (65.58–133.25)	1.08 (0.08–3.75)	2.77 (0.95–5.72)
MUCS	Bg	68	12.69 (6.85–22.75)	86.76 (54.96–168.04)	0.71 (0.02–4.31)	0.88 (0.01–5.25)
	B	33	14.57 (5.83–33.64)	113.89 (39.82–222.39)	4.10 (0.49–34.17)	3.55 (0.79–15.77)
	I	17	13.61 (7.65–33.78)	92.83 (33.49–168.04)	5.05 (1.44–24.09)	3.87 (0.79–12.07)

(*N*) Sample size, (Bg) background zone, (B) buffer zone, (I) impact zone.

Table 3. Sizes of samples used to analyze FA in the mandible shape in bank voles from industrial pollution gradients and background areas

Emission source	Number of animals from zones with different levels of industrial pollution		
	impact zone	buffer zone	background zone
KCS	16	–	33
KCSW	7	80	13
MUCS	24	26	55
Shigaevo (external control)		21	

used the sample of bank voles trapped in 2006 near the village of Shigaevo (the Middle Urals), where the pollution load is at the global background level (Gileva et al., 2006). Data on the total amount of material from the gradients of industrial pollution in the Middle and Southern Urals are presented in Table 3.

The samples of voles included males and females of three age classes of cranial maturity estimated by the alveolar tubercle development of the second upper molar in the sphenoorbital foramen (Razorenova, 1952). The validity of this approach to determining the relative age of animals in morphological studies on voles of the genus *Clethrionomys* has been confirmed previously (Fominykh, 2011).

Analysis of FA was performed in digital images of the right and left mandible segments from the lingual side using the method of geometrical morphometry in the TPS program package (Rohlf, 2003a, b). Images were taken under a Carl Zeiss Stemi-2000-C microscope (at a 6.5× magnification) with a Nikon Coolpix 4500 digital camera, with the position of the mandible being strictly standardized. Twelve landmarks were pointed on the images of each hemimandible (in two replicates) that described the shape of the anterior (diastemal) module (landmarks 3–8) and the posterior module (landmarks 1, 2, 8–12) (Fig. 1).

Further analysis followed the procedure proposed by Palmer and Strobeck (2003) and modified as required for geometrical morphometry (Klingenberg and McIntyre, 1998). The values of FA were calculated from the Procrustes coordinates (x, y) of the marks representing the differences between coordinates of the best fit landmark configuration and the corresponding superimposed landmarks after the Procrustes procedure. The superimposition procedure involved reduction of the landmarks on the left and right hemimandible to a single configuration by mirror-imaging one of the hemimandible and then using the least-squares method to minimize differences in the positions of all landmarks between all configurations (Bookstein, 1991; Klingenberg and McIntyre, 1998). This procedure allowed us to eliminate differences in the configuration of the landmarks that resulted from differences in the size of the mandibles and their position during imaging.

A Procrustes ANOVA (Klingenberg and McIntyre, 1998) was performed to estimate the presence of directional asymmetry and the significance of FA relative to the measurement error. This analysis was based on the results of two-way ANOVA (mixed model: “side” is a fixed factor, “individual” is a random factor; repeated measurement—is an observation in the plan cell). The sums of squares calculated for the x and y coordinates

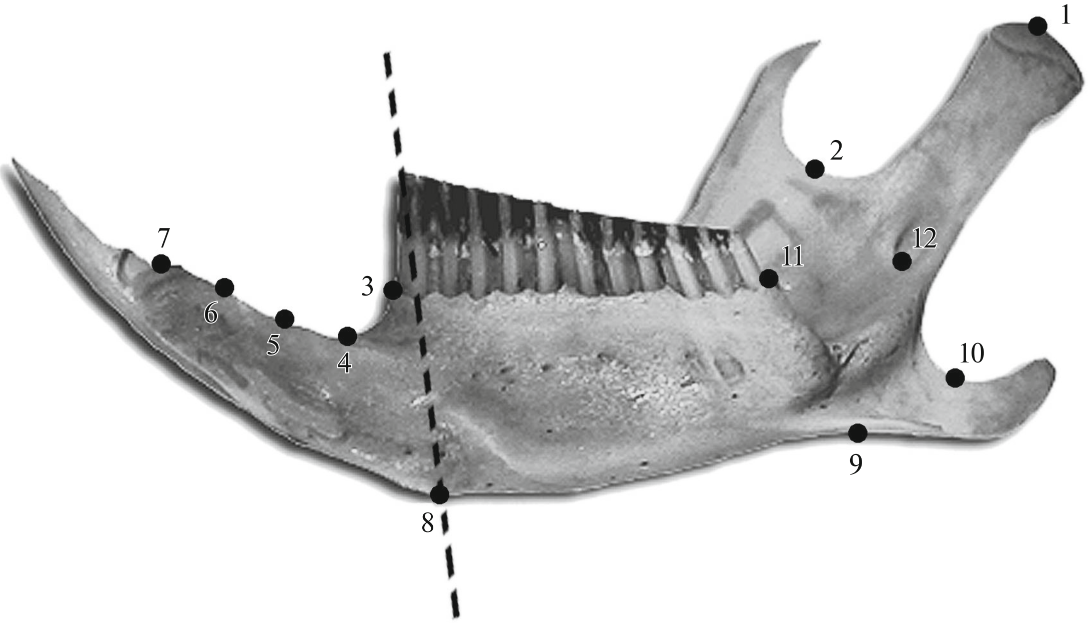

Fig. 1. Locations of marks on the *Cl. glareolus* mandible: (1) the apex of the condylar process, (2) the deepest point between the condylar and coronoid processes, (3) the anterior edge of /m1 alveolus, (4, 5, 6) semi-landmarksa characterizing the geometry of the mandibular diastema, (7) the anterior edge of the incisor alveolus, (8) symphyseal tubercle, (9) the deepest point at the base of the angular process, (10) the deepest point in the bend of the angular process, (11) the posterior edge of /m3 alveolus, (12) the lower edge of the mandibular foramen. The dashed line shows the boundary between the modules.

were summed up for all the landmarks and for each mandible module separately, thereby obtaining the Procrustes sum of squares for each effect ("side," "individual", interaction "side × individual," error). To calculate the degrees of freedom for Procrustes ANOVA, their number for each effect was multiplied by the doubled number of summed-up lanmarks minus four (the total number of summed-up coordinates minus four for Procrustes superimposition). The mean square for each effect was calculated by dividing the Procrustes sum of squares by the corresponding number of the degrees of freedom. The calculated mean squares and degrees of freedom were used to test for the statistical significance of effects (F-test); the mean square of the interaction between factors "side" and "individual" was used to estimate the significance of effects of factors "individual" and "side", and the mean square of error, to estimate the significance of the effect of the interaction. The results of Procrustes ANOVA provided evidence for the presence of directional asymmetry (the effect of factor "side" is statistically significant, $P < 0.001$) and of FA that exceeds the measurement error (the effect of interaction "individual × side" is also significant, $P < 0.001$). Testing for normality of distribution of FA indices for the two mandible modules by Kolmogorov–Smirnov method recommended for small samples (Palmer, 1994) showed the absence of antisymmetry ($P \geqslant 0.20$). The index FA18 used as the integral characteristic of FA of the shape of the anterior and posterior mandible modules in each individual was calculated as follows (Palmer and Strobeck, 2003):

$$\mathrm{FA18}=\sqrt{(R_x - L_x)^2 + (R_y - L_y)^2},$$

where R_x and R_y are the coordinates of a landmark on the right side of mandible, and L_x and L_y are its coordinates on the left side of mandible.

The results were processed statistically using the Statistica v. 6.0 for Windows program package (StatSoft Inc., 1984–2001). Statistical hypotheses were tested at the 5% significance level.

RESULTS AND DISCUSSION

Samples from two model plots in the impact zone of MUCS and the background zone of KCSW included bank voles trapped in different years. The integral indices of FA for the two mandible modules did not differ between years ($P \geqslant 0.379$), which allowed us to pool the data obtained in different years for subsequent analysis. Taking into account the necessity of a detailed examination of samples from natural populations because of their possible heterogeneity in parameters that can affect evaluation of FA (Gileva and Nokhrin, 2001), we performed data analysis to reveal possible differences between our samples depending on their age and sex composition.

The samples did not differ in the male-to-female ratio ($P < 0.05$). Two-way ANOVA with factors "sex" and "age" for FA18 of the anterior and posterior man-

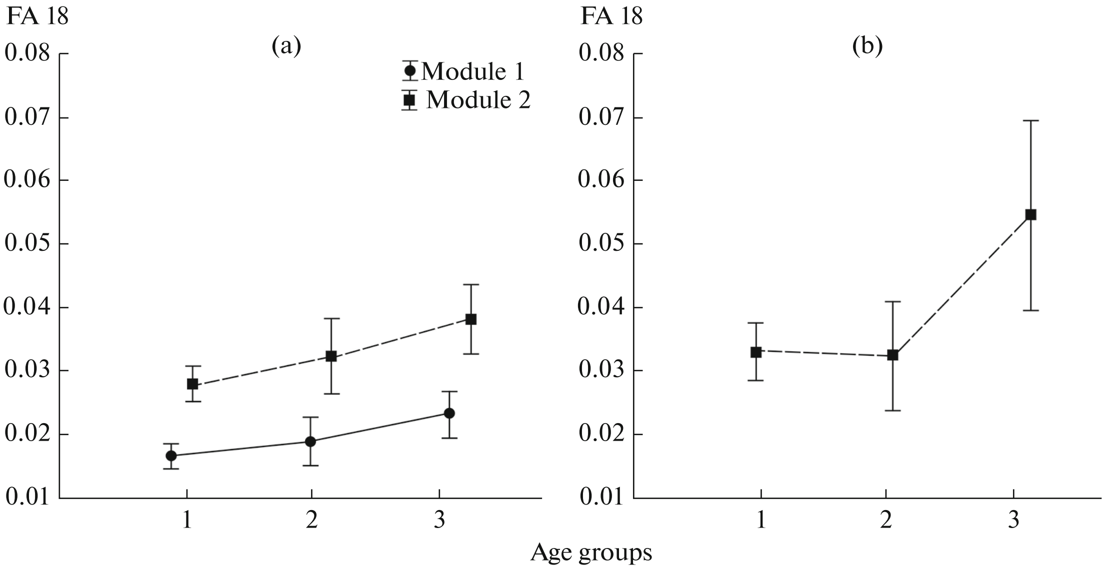

Fig. 2. Average FA18 values for (a) two mandible modules in bank voles of different age groups from the MUCS background zone and (b) the posterior module in voles from the external control zone.

dible modules revealed no significant effect of the factor “sex” in any of the samples ($P > 0.05$). The effect of factor “age” was significant in both modules in voles from the background zone of MUCS ($F_{2/49}$ = 4.863, $P = 0.012$ and $F_{2/49}$ = 4.998, $P = 0.011$ for the anterior and posterior modules, respectively) and for the posterior module in voles from Shigaevo ($F_{2/15}$ = 4.822; $P = 0.024$). Pairwise comparisons of different age groups from these localities showed that the significance of this effect was explained by significantly higher FA18 values in voles of the older age group (class 3 of cranial maturity) than in younger voles (classes 1 and 2) (Fig. 2).

The influence of age on FA in mammals has been demonstrated for both metrical and meristic characters. In particular, FA in rodents has been found to decrease with age (Siegel et al., 1977; Parker and Leamy, 1991; Novak et al., 1993; Vasil’ev et al., 1996), but the inverse situation has also been observed (Gileva and Nokhrin, 2001). The relationship between the processes of growth and morphogenesis in the postnatal period is apparently complex and needs special study involving an analysis of representative samples from all age groups. To minimize the contribution of age variability in FA, subsequent analysis was performed only with animals of classes 1 and 2.

FA values of the two modules of the mandible in samples from industrial pollution gradients of the three copper smelters were compared using two-way ANOVA with factors “locality” and “module” (FA18 values of the first and second modules were regarded as a repeated measurements). The effects of both factors were highly significant ($F_{8/257}$ = 2.577, $P = 0.010$ and $F_{1/257}$ = 400.658, $P < 0.001$, respectively), unlike the effect of factors interaction ($F_{8/257}$ = 0.570, $P = 0.802$).

In all the samples, regardless of the magnitude of technogenic impact, FA18 values for the second module proved to be twice or more higher than those for the diastemal region (Fig. 3). Therefore, the previously described differences in FA of shape between the bank vole mandible modules distinguished by morphofunctional criteria (Yalkovskaya et al., 2014) can

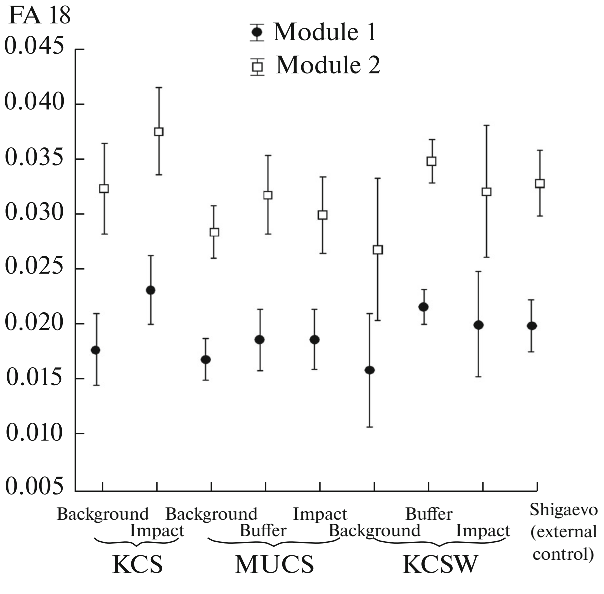

Fig. 3. Average FA18 values for two mandible modules in bank voles from industrial pollution gradients in the Urals.

also be traced in natural areas with different levels of industrial pollution.

It is not readily obvious that differences between the samples in FA18 values for the two mandible modules in bank voles are conditioned by the level of technogenic load on their habitats. Thus, comparisons of FA in animals from the vicinities of copper smelters with the external control showed that FA18 values for the mandible modules in bank voles from Shigaevo are similar to or even higher than in animals from the impact and buffer zones of the pollution gradients. However, since FA is a complex phenomenon, the sample from Shigaevo can only tentatively be regarded as a control for the samples from the zones of MUCS, KCSW, KCS, because the territory of this village lies beyond any of the tree pollution gradients. Taking into account that differences in FA revealed in comparisons of samples from relatively distant populations may not necessarily be due to different levels of technogenic impact, further analysis of FA18 values depending on the degree of industrial pollution was performed with regard to the location of sampling sites in a certain local gradient.

Comparisons o FA in samples from local gradients were made for each mandible module separately using ANOVA with factors "plant" (MUCS, KCS, and KCSW) and "zone" (impact, buffer, and background). For the diastemal region, the effect of factor "zone" was significant ($F_{2/186} = 3.751$, $P = 0.025$), while effect of the factor "plant" and the interaction of these factors lacked statistical significance ($F_{2/186} = 2.623$, $P = 0.075$ and $F_{3/186} = 0.607$, $P = 0.611$, respectively). For the posterior module, the interaction of the two factors also had no significant effect ($F_{3/186} = 0.647$, $P = 0.586$), but the effect of factor "plant" was significant ($F_{2/186} = 6.414$, $P = 0.002$), as well as that of the factor "zone" ($F_{2/186} = 5.362$, $P = 0.005$).

Comparative analysis of FA in both mandible modules in samples from the impact, buffer, and background zones revealed a pattern common to all the three pollution gradients (Fig. 3): FA18 values were the lowest in the background zones of the smelters, but they increased under significant technogenic load in the impact zones, and the values recorded at pollution levels of the buffer zones proved to be comparable to (or even slightly higher than) in samples from the impact zones. Therefore, an increase in ontogenetic instability in response to increasing technogenic impact is manifested within local gradients of industrial pollution, i.e., under conditions of high uniformity between model plots with respect to parameters of topography, climate, soils, vegetation, etc.

The significance of differences in FA18 for the posterior module between local pollution gradients is due to the high FA18 values in voles from the impact zone of KCS (the Southern Urals), compared to MUCS and KCSW (the Middle Urals). This is additional evidence that the effect of industrial pollution on the degree of ontogenetic instability should be evaluated under conditions of maximum identity of other environmental factors.

As a result of this study, we have estimated the levels of FA of the shape of the mandible in bank voles from industrial pollution gradients around thee copper smelters in the Urals. It has been shown that there is the necessity for a detailed analysis of the material from natural populations, since the level of ontogenetic instability may depend on population parameters, animal age in particular. Differences between the two mandible modules (distinguished by the criteria of functional load, the sequence of ontogenetic processes, and patterns of FA) are manifested both under exposure to strong technogenic impact and under background conditions. The value of integrated FA index for the posterior module (including the lower part of mandibular body, ramus and mandibular processes) is twice or more higher than that for the anterior (diastemal) module, regardless of pollution level.

A comparative analysis of bank vole samples with respect to FA values of both mandible modules depending on the level of technogenic impact has revealed a gradient effect of toxic exposure on ontogenetic homeostasis in rodents from natural populations. Disturbance of developmental stability in response to increase in industrial pollution is clearly manifested within local gradients of industrial poluttion, with pollution levels characteristic of buffer zones providing for an increase in FA to values observed near the sources of emissions.

These data should be taken into account in studies on the assessment of technogenic impact and ecological monitoring with the use of FA indices as indicators of ontogenetic homeostasis. Special attention should be given to the choice of indicator characters, uniformity of samples from natural populations with respect to parameters that can affect the results of research, and careful selection of model plots for adequate comparative analysis.

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