# Biodistribution of $^{99m}$Tc-$O_4$Na Changes in Adult Rats Whose Mothers Were Malnourished During Lactation

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$^{99m}$Tc-$O_4$Na biodistribution changes in malnourished adults rats. We evaluated this biodistribution in rats whose mothers were malnourished during lactation. **Methods:** On the first day of lactation the mothers were separated into 3 groups: control (C) group, protein-restricted (PR) group, and energy-restricted (ER) group. After weaning all pups received a control diet until 60 d, when they were injected with $^{99m}$Tc-$O_4$Na and killed after 30 min. We evaluated the absolute percentage injected dose (%ID) and the %ID per gram (%ID/g) in thyroid, stomach, heart, bone, kidney, lung, liver, brain, and testes. **Results:** In the PR group, the %ID and %ID/g were significantly higher in the stomach and lower in the thyroid than in the C group. In the ER pups, the %ID and %ID/g were higher in the liver, stomach, and testes than in the C group. **Conclusion:** The mother's nutritional status during lactation affects the biodistribution of $^{99m}$Tc-$O_4$Na in the offspring, and this condition must be considered when nuclear medicine examinations are indicated.

**Key Words:** protein restriction; energy restriction; lactation; $^{99m}$Tc-$O_4$Na

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Malnutrition is the most prevalent form of nutritional disorder among children in developing countries. Protein malnutrition often occurs during gestation, lactation, and the first 2 y of life in humans. Besides the economic factors, the nutritional habits and lack of nutritional guidance lead to a high prevalence of this type of malnutrition during gestation or lactation (or both) in developing countries. In affluent populations, breast-feeding women often wish to return to their weight before pregnancy as soon as possible and, during lactation, may restrict food intake without nutritional guidance to achieve this goal.

Some studies have shown that lactation could be a critical period for the future nutritional and hormonal status of the progeny, a relationship that has been termed metabolic imprinting (*1*). We have shown that protein malnutrition during lactation is associated with thyroid dysfunction in the dams (*2*) and that the mother's nutrition during lactation can determine the body weight of their offspring in adult life, which can be associated primarily with protein and lipid milk concentration (*3*).

Iodide and $^{99m}$Tc as $^{99m}$Tc-$O_4$Na are used primarily for thyroid scintigraphy, although they also can be used for cerebral evaluations in nuclear medicine procedures. Conditions that modify the uptake of these radiopharmaceuticals may produce misleading interpretations of nuclear medicine examinations because of poor organ visualization or false-negative results. This may result in the necessity to repeat examinations, resulting in unnecessary irradiation of the organs (*4*).

We reported recently that the biodistribution of $^{99m}$Tc-$O_4$Na changes in malnourished adults rats (*5*). Because protein malnutrition often occurs during lactation, we evaluated the biodistribution of $^{99m}$Tc-$O_4$Na in rats after weaning whose mothers received protein-restricted (PR) or energy-restricted (ER) diets during lactation, thus characterizing another example of metabolic imprinting.

## MATERIALS AND METHODS

Wistar rats obtained from the animal facilities of Oswaldo Cruz Institute (Rio de Janiero, Brazil) were kept in a room with controlled temperature (25°C ± 1°C) and with artificial dark–light cycles (lights on from 7:00 AM to 7:00 PM). Two virgin female rats (3 mo old) were caged with 1 male rat. After mating, each female was placed in an individual cage with free access to water and food

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**TABLE 1**
Composition of Diets

| Parameter | Diet | | |
|---|---|---|---|
| | C* | PR† | ER‡ |
| Ingredients (g/kg) | | | |
| Soybean + wheat | 230.0 | 80.0 | 230.0 |
| Cornstarch | 676.0 | 826.0 | 676.0 |
| Soybean oil | 50.0 | 50.0 | 50.0 |
| Vitamin mixture§ | 4.0 | 4.0 | 4.0 |
| Mineral mixture§ | 40.0 | 40.0 | 40.0 |
| Macronutrient composition (%) | | | |
| Protein | 23.0 | 8.0 | 23.0 |
| Carbohydrate | 66.0 | 81.0 | 66.0 |
| Fat | 11.0 | 11.0 | 11.0 |
| Total energy (kJ/kg) | 17,038.7 | 17,038.7 | 17,038.7 |
| Mean energy intake (kJ/d) | 512.2 | 311.8 | 311.8 |

*Standard (control) diet for rats (Nuvilab-NUVITAL Nutrientes LTDA, Paraná, Brazil).

†PR (low protein) diet was prepared in our laboratory using C diet and replacing part of its protein with cornstarch. Amount of the latter was calculated to make up for decrease in energy content associated with protein reduction.

‡Standard laboratory diet in restricted quantities.

§Vitamin and mineral mixtures were formulated to meet American Institute of Nutrition recommendation AIN-93G for rodent diets.

until delivery. Use of the animals according to our experimental design was approved by the Animal Care and Use Committee of the Biology Institute of the University of the State of Rio de Janeiro.

Dams were randomly assigned to 1 of the following groups: control (C) group, with free access to a standard laboratory diet containing 23% protein; PR group, with free access to an isoenergy and protein-restricted diet containing 8% protein; and ER group, which received a standard laboratory diet in restricted quantities that were calculated according to the mean ingestion of the PR group. In this way, the amounts of food consumed by the ER and PR groups were about the same. Table 1 shows the composition of the diets.

Within 24 h of birth, excess pups were removed, so that only 6 male pups were kept per dam because this procedure maximizes lactation performance. Malnutrition was started at birth, which was defined as day 0 of lactation, and was ended at weaning (day 21).

After weaning, all pups received free access to the C diet, until 60 d, when they received 0.3 mL $^{99m}$Tc-$O_4$Na (7.4 MBq) through the ocular plexus (Nuclear Medicine Service, Pedro Ernesto University Hospital, University of the State of Rio de Janeiro). After 30 min, the animals were quickly killed. The organs were isolated (thyroid, brain, lungs, heart, kidney, liver, stomach, testes, and bone), their weights were determined, and the radioactivity of the $^{99m}$Tc-$O_4$Na was counted in a NaI(Tl) well counter (Cobra Autogamma; Packard Instrument Co., Downers Grove, IL). The absolute percentage injected dose (%ID) and the %ID per gram of tissue (%ID/g) were determined for each organ. Statistical analyses were performed using 1-way ANOVA followed by the Newman–Keuls, multicomparison test. $P < 0.05$ was considered significant.

## RESULTS

The biodistribution of $^{99m}$Tc-$O_4$Na and the weights of the isolated organs of pups whose mothers were submitted to a PR or ER diet during lactation are shown in Table 2. Except for a significant decrease (12%) in the weight of the brain of pups of PR mothers, the weight of other organs did not change.

The %ID/g and %ID increased in the stomach (87 %ID/g and 65 %ID) and decreased in the thyroid (33 %ID/g and 48 %ID) but did not change significantly in the heart, kidney, lung, liver, bone, brain, or testes of pups of PR mothers. In pups of ER mothers, the %ID and %ID/g showed a signif-

**TABLE 2**
$^{99m}$Tc-$O_4$Na Biodistribution (%ID/g and %ID) and Organ Weight of Pups

| Organ | Group | | | |
|---|---|---|---|---|
| | C diet* | PR diet* | ER diet* | *P* |
| Thyroid | | | | |
| %ID/g | 505 ± 152 | 336 ± 58†‡ | 725 ± 174 | 0.05 |
| %ID | 7.1 ± 1.1 | 3.7 ± 0.7†‡ | 8.2 ± 0.8 | 0.05 |
| Weight (g) | 0.010 ± 0.001 | 0.007 ± 0.001 | 0.011 ± 0.002 | NS |
| Stomach | | | | |
| %ID/g | 50 ± 6 | 94 ± 7† | 94 ± 4† | 0.01 |
| %ID | 70.7 ± 5.1 | 117.0 ± 5.8†‡ | 150.0 ± 11.4† | 0.05 |
| Weight (g) | 1.42 ± 0.14 | 1.25 ± 0.10 | 1.60 ± 0.01 | NS |
| Heart | | | | |
| %ID/g | 4.3 ± 0.5 | 3.7 ± 1.3 | 5.1 ± 0.3 | NS |
| %ID | 3.5 ± 0.3 | 2.9 ± 0.6 | 4.2 ± 0.5 | NS |
| Weight (g) | 0.82 ± 0.05 | 0.79 ± 0.09 | 0.82 ± 0.06 | NS |
| Bone | | | | |
| %ID/g | 6.3 ± 0.7 | 4.2 ± 0.9 | 6.1 ± 0.6 | NS |
| %ID | 2.6 ± 0.3 | 1.7 ± 0.5 | 2.7 ± 0.3 | NS |
| Weight (g) | 0.41 ± 0.04 | 0.40 ± 0.02 | 0.44 ± 0.02 | NS |
| Kidney | | | | |
| %ID/g | 14.7 ± 2.0 | 16.6 ± 1.3 | 19.3 ± 1.8 | NS |
| %ID | 12.9 ± 0.9 | 12.9 ± 1.2 | 15.0 ± 1.2 | NS |
| Weight (g) | 0.91 ± 0.09 | 0.77 ± 0.04 | 0.78 ± 0.03 | NS |
| Lung | | | | |
| %ID/g | 8.3 ± 1.9 | 6.7 ± 1.3 | 12.9 ± 3.1 | NS |
| %ID | 3.7 ± 0.9 | 2.7 ± 0.8 | 5.5 ± 1.2 | NS |
| Weight (g) | 0.45 ± 0.09 | 0.40 ± 0.06 | 0.43 ± 0.07 | NS |
| Liver | | | | |
| %ID/g | 8.3 ± 1.1 | 7.8 ± 1.0‡ | 12.7 ± 0.9† | 0.05 |
| %ID | 10.1 ± 0.6 | 13.3 ± 1.8‡ | 18.6 ± 2.1† | 0.01 |
| Weight (g) | 1.25 ± 0.14 | 1.70 ± 0.15 | 1.50 ± 0.14 | NS |
| Brain | | | | |
| %ID/g | 0.53 ± 0.20 | 0.40 ± 0.04 | 0.50 ± 0.06 | NS |
| %ID | 0.90 ± 0.3 | 0.60 ± 0.07 | 0.80 ± 0.09 | NS |
| Weight (g) | 1.70 ± 0.01 | 1.50 ± 0.02† | 1.60 ± 0.05 | 0.05 |
| Testes | | | | |
| %ID/g | 2.5 ± 0.2 | 2.6 ± 0.4‡ | 3.8 ± 0.3† | 0.05 |
| %ID | 3.0 ± 0.5 | 2.9 ± 0.5‡ | 4.6 ± 0.4 | 0.05 |
| Weight (g) | 1.20 ± 0.12 | 1.10 ± 0.10 | 1.20 ± 0.08 | NS |

*Mean ± SD of 10 animals.

†Significant differences between diet-restricted groups and control group.

‡Significant differences between 2 diet-restricted groups.

NS = not significant.

icant increase in the liver (53 %ID and 84 %ID/g) and stomach (86 %ID and 112 %ID/g), and in the testes only the %ID/g increased significantly (52 %ID/g) compared with that in the C group. The %ID/g and %ID did not change in the other organs.

## DISCUSSION

The nutritional status of mothers during lactation can affect $^{99m}$Tc-$O_4$Na biodistribution in different organs of the offspring, and those changes differ according to the kind of malnutrition. Although the mother's malnutrition affected the $^{99m}$Tc-$O_4$Na biodistribution in the offspring, it did not alter the organ weight, except for a decrease in the weight of the brain.

Substitution of $^{99m}$Tc-$O_4$Na for iodine radioisotopes is being used increasingly for thyroid scintigraphy and is useful for identification of thyroid diseases because its uptake by the thyroid is similar to that of iodine. We found that the animals that were fed a normal diet after weaning but whose mothers had PR diets during lactation had a decrease in $^{99m}$Tc-$O_4$Na thyroid uptake. These results reinforce our previous findings showing that protein malnutrition is always associated with a decrease in $^{131}$I or $^{99m}$Tc-$O_4$Na thyroid uptake, in spite of the animal's age (*2*,*5*). It is possible that the protein restriction is associated with reduction in the transcriptional activity of the sodium iodine symporter because this protein can transport iodine and $^{99m}$Tc-$O_4$Na.

As in the adult PR animals (*5*), there was an increase in $^{99m}$Tc-$O_4$Na uptake in the stomach that cannot be explained by the marked decrease in $^{99m}$Tc-$O_4$Na uptake in the thyroid of pups of PR mothers, because the amount of tracer that was not taken up by the thyroid was almost 10 times lower than the amount that increased in the stomach's uptake. Furthermore, the animals whose mother was ER during lactation did not show any change in thyroid $^{99m}$Tc-$O_4$Na uptake but did show a similar degree of increase in the $^{99m}$Tc-$O_4$Na uptake in the stomach. This increase may be related to an increase in the stomach's velocity or circulation, which could increase the stomach's function.

The results of this study show that energy restriction during lactation leads to different alterations in the biodistribution of radiopharmaceutical in the offspring compared with that observed in protein restriction. This observation reinforces our previous findings in adult animals (*5*).

## CONCLUSION

This study suggests that lactation could be a critical period that determines future changes in the biodistribution of radiopharmaceutical compounds of the progeny, thus characterizing another example of metabolic imprinting. Therefore, the nutritional status of mothers during lactation must be considered when nuclear medicine examinations are indicated because this condition may produce false-positive results.


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