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Activity Pattern of Iron-Deficient Rats

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Summary

Iron-deficient rats appear to have a decrease in total activity and a disorder of diurnal rhythm. These are reversed by the administration of iron. The results may be relevant to the symptomatology of patients with iron deficiency anaemia.

Introduction

The symptoms of iron deficiency anaemia are difficult to define in objective terms. Although most accounts of the disease describe tiredness, weakness, irritability, and other non-specific manifestations it has not been possible to substantiate these in studies based on questionnaires and simple tests of psychomotor function (Elwood *et al.*, 1969; Elwood and Hughes, 1970).

We have used an apparatus for the continuous monitoring of rat movements to measure total daily activity and the diurnal rhythm in normal and iron-deficient rats. The results of a pilot study show that deviations from normal are found in iron-deficient animals and that they are rapidly reversed by the administration of iron.

Methods

An Animex activity meter (L.K.B. Ltd.) was used to monitor total and large movements of groups of rats. Each group of three rats was placed in a standard Perspex cage which rested on six high-frequency oscillator coils. The oscillator circuit was tuned for each group of rats. The movements of the rats within the electromagnetic field produced by the apparatus resulted in an alteration of the tuning and this is registered by a scaler (Svensson and Thieme, 1969; Ogran, 1970). Two recording channels were used, one tuned for large movements and one for total movements. Small movements were found as the difference between the two.

Three groups of six male Wistar rats of similar weights were studied. In each group three rats were killed for the establishment of initial haematological criteria and three were monitored for activity. Standard haematological methods were used.

Group 1.—Normal iron status. Rats maintained on a standard diet (41B) since weaning. Activity was monitored for six days.

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Ferric ammonium sulphate was given in the drinking water on days 3 and 4 (28 mg/100 ml).

Group 2.—Iron deficiency anaemia. Rats maintained on an iron-free diet (McCall *et al.*, 1962) since weaning. Activity was monitored for seven days. Ferric ammonium sulphate was given in the drinking water on days 4 and 5.

Group 3.—Mild iron deficiency anaemia. Rats maintained on an iron-deficient diet since weaning. Anaemia partially corrected by four days on normal diet given 10 days before the start of the experiment. Activity was monitored for six days. Ferric ammonium sulphate was given in the drinking water on days 3 to 6.

Access to the animal room was strictly limited during activity measurements. Large and total movements were recorded separately for consecutive 30-minute periods throughout the period of observation.

Results

The characteristics of each group of rats are shown in the Table. There was a considerable reduction in the total number of movements in both the mildly and severely iron-deficient rats. Large and small movements were equally affected. The effect of

Characteristics of the three Groups of Rats

	Group 1	Group 2	Group 3
Weight (g)	245.0	209.0	323.0
Haemoglobin (g/100 ml)	14.6	5.0	12.0
Packed cell volume (%)	47.0	21.0	41.0
Red cell count ($\times 10^6$ /l.)	7.9	6.9	7.8
M.C.H.C. (%)	31.0	24.0	29.0
M.C.V. (μm^3)	60.0	30.0	53.0
Serum iron (g/100 ml)	266.0	19.0	76.0
Total iron binding capacity (g/100 ml)	375.0	712.0	730.0
Liver non-haem (mg/100g tissue)	12.0	0.9	2.1
Total small movements in 24 hours	49,000	23,000	24,000

Each value is the mean of three rats. Total movements are the mean of a number of days' activity before treatment (see text).

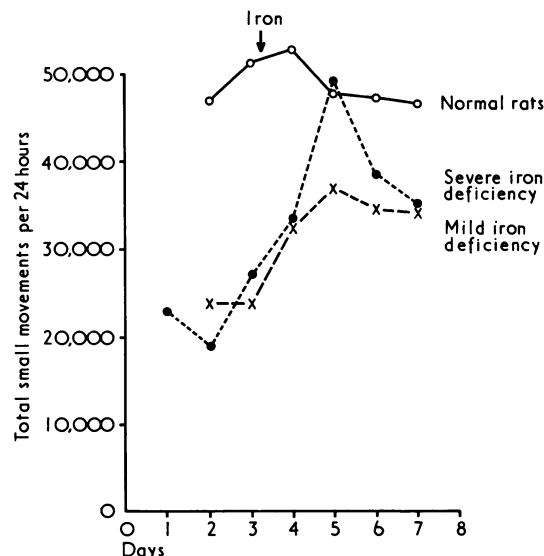


FIG. 1—Changes in activity after administration of iron in the three groups of rats.

administering iron is shown in Fig. 1. In normal rats there was no significant change in activity. In severely iron-deficient rats there was a pronounced increase in activity after iron was given but a decline towards previous levels in the two days after iron was withheld. In the mildly anaemic rats iron administration was continued and there was a smaller but sustained increase in activity.

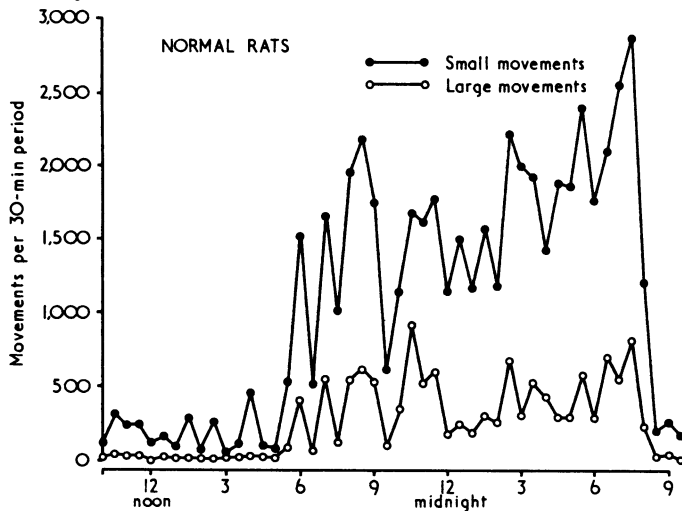


FIG. 2—Diurnal activity pattern in normal rats.

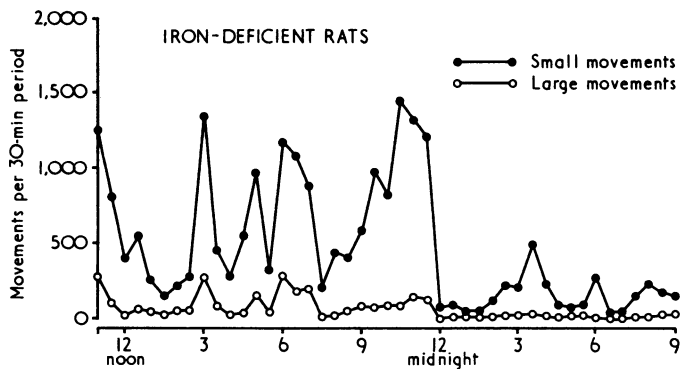


FIG. 3—Diurnal activity pattern in iron-deficient rats.

The normal diurnal pattern of rat activity is shown in Fig. 2. The animals were normally fully awake during the hours of darkness and asleep during daylight. A typical activity pattern in the iron-deficient rats is shown in Fig. 3. There was a noticeable alteration in the diurnal rhythm, with a high proportion of the day's activity taking place during the hours of daylight and a cessation of activity at about midnight. This pattern was repeated in each daily cycle and was seen in both iron-deficient groups. A group of mildly anaemic rats given an iron supplement did not show any reversion to a normal cycle until seven to eight days after therapy was started.

Conclusions

The present pilot study indicates a pronounced change in behaviour in iron-deficient rats consisting partly in a reduction of total activity and partly in an alteration of diurnal rhythm. The cause of this abnormality is unknown but it appears to be rapidly corrected by the administration of iron.

Beutler *et al.* (1960) suggested that symptoms in iron deficiency may be related to depletion of tissue iron enzymes, and these are known to exist in both animal and human subjects (Jacobs, 1969). Patients with iron deficiency anaemia appear to show behaviour changes which often seem to revert to normal after treatment, but it has been difficult to measure this phenomenon, and indeed some have doubted its existence (Elwood *et al.*, 1969). The observation of abnormal behaviour in iron-deficient rats is of interest in this context. The possibility of defining behaviour changes in human iron deficiency awaits the introduction of appropriate techniques.

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MEDICAL MEMORANDA

Breast Abscess: A Rare Presentation of Typhoid

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Case Report

A 43-year-old nulliparous woman was admitted to hospital via the casualty department with a three-week history of high fever and malaise. One day before admission she developed pain in the right breast. There had been no discharge from the nipple and

and there was no previous history of breast disease. She had not had diarrhoea, constipation, or a urinary abnormality, had not been abroad, and had never had a T.A.B. inoculation.

On examination she was found to be pyrexial (temperature 104°F; 40°C), and had a tachycardia of 120/min. Above and lateral to the right nipple there was a warm, tender, and hard lobulated mass which measured 5 cm in diameter. The skin was erythematous and adherent to the mass but the mass was not tethered deeply. The nipple was not retracted and there was no discharge. The respiratory, alimentary, nervous, and musculo-skeletal systems showed nothing abnormal.

The differential diagnosis rested between a breast abscess and an inflammatory carcinoma with or without a secondary infection. She was submitted to drill biopsy, and at operation a little pus was drained from a firm, indurated mass. Histologically the specimen showed acute inflammation of breast tissue.

Investigations were: haemoglobin 12.1 g/100 ml; W.B.C. 12,900/mm³ (79% neutrophils); E.S.R. 62 mm in 1 hour; wound swab culture, pure growth of *Salmonella typhi*; blood culture, no growth; Widal test, *Salm. typhi* H 1/800, O 1/800, Vi 1/160, untypable Vi strain (Enteric Reference Laboratory), *Brucella abortus* 1/25. Ten days later the titre of the *Salm. typhi* H was 1/400; apart from this there was no change. No pathogens were

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