Development of stereotypies and polydipsia in wild caught bank voles (*Clethrionomys glareolus*) and their laboratory-bred offspring. Is polydipsia a symptom of diabetes mellitus?

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Abstract

The development of stereotypies and polydipsia was studied in wild caught bank voles (P: *n* = 92) and their laboratory-bred offspring (F1: *n* = 248). All animals were kept isolated in barren cages in the laboratory. In the P generation, no individuals developed stereotypies, but 22% developed polydipsia (> 21 ml/day water intake against normally 10 ml/day). Polydipsia was more frequent among males (34%) than females (13%). In F1, 30% developed locomotor stereotypies alone, 21% showed polydipsia alone, and, additionally, 7% developed both stereotypies and polydipsia. Fewer males than females developed stereotypies (23% vs. 38%), whereas polydipsia was more frequent in males than in females (30% vs. 11%). The occurrence and distribution of polydipsia among sexes were the same in F1 and P. The distribution of different types of stereotypies in stereotyping voles were backward somersaulting (BS, 80%), high-speed jumping (JUMP, 29%), pacing following a fixed route (PF, 12%) and windscreen wiper movement (WIN, 5%). Some individuals (10%) showed two or more different types of stereotypies. The average age for developing stereotypies was 96 days while polydipsia was registered at the age of 63 days in both sexes. Voles showing both polydipsia and stereotypies developed polydipsia later (79 days) than polydipsic voles not showing stereotypies. This difference was especially pronounced in stereotyping females in which the occurrence of polydipsia was postponed to the age of 114 days. Polydipsic voles were tested positive for glucosuria indicating...
that polydipsia could be a symptom of diabetes mellitus. It is suggested that the development of stereotypies and polydipsia among bank voles in the laboratory are the results of frustration and prolonged stress. Stereotypies seem to depend on frustrative experiences early in life, while polydipsia may be related to diabetes mellitus caused by the experience of prolonged stress. Moreover, circumstances related to the development of stereotypies may be adaptive by reducing the risks of prolonged stress, including the development of fatal polydipsia. © 2000 Elsevier Science B.V. All rights reserved.

**Keywords:** Bank voles; Stereotypies; Polydipsia; Diabetes mellitus; Adaptive value

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1. **Introduction**

Stereotypies are the collective term for a group of phenotypic different behaviours that share the following three characteristics: Morphologically identical movements, which are repeated regularly and have no obvious function (Ödberg, 1978). Stereotypies occur in many different species kept in captivity or intensive husbandry and farms (Mason, 1991). Stressors like barren environments (Sørensen, 1987), scheduled and restricted feeding (Falk, 1969, 1971; Bildsøe et al., 1991; Lawrence and Terlouw, 1993), social deprivation (Sahakian et al., 1975; Broom, 1983; Arellano et al., 1992), frustration (Feldman, 1978; Ödberg, 1978; Rushen, 1985; Ödberg, 1987) and tethering (Cronin et al., 1985a) are generally associated with stereotypies. The eliciting circumstances, the ontogeny, and the context in which stereotypies are performed are very heterogenic (Cronin et al., 1985b; Mason, 1991, 1993). Laboratory-bred, but not wild caught, bank voles housed in barren cages develop spontaneous locomotor stereotypies with a high frequency (Ödberg, 1986). The voles perform easily recognisable stereotypies such as backward somersaulting (BS), jumping, pacing following a fixed route (PF) and windscreen wiper movement (WIN) (Sørensen and Randrup, 1986; Ödberg, 1986; Sørensen, 1987; Cooper and Nicol, 1991, 1996). Increasing the size and complexity of the housing conditions reduces the incidence of stereotypies in bank voles (Ödberg, 1987), but old voles show stronger perseverance of stereotypies than younger voles after environmental enrichment (Cooper and Nicol, 1996). Moreover, there seems to be no difference in mortality or fecundity between laboratory-bred and wild caught voles (Cooper and Nicol, 1996).

Both wild caught and captivity-bred bank voles have been reported to develop excessive drinking or polydipsia in the laboratory (Sørensen and Randrup, 1986), but the causes of this abnormality, its ontogeny and its relation to the occurrence of locomotor stereotypies is uncertain. Likewise, there is no detailed information on possible sex differences in the development of stereotypy and polydipsia, just as we know only a little about mortality especially in polydipsic voles.

The present study aimed at examining the development of stereotypic behaviour and polydipsia in wild caught bank voles and their laboratory-bred offspring when kept isolated under barren housing conditions. Attention was specifically paid to associations with age and sex. Moreover, the possibility that polydipsia in bank voles could be a symptom of diabetes mellitus was preliminary tested (Ganong, 1991).
2. Materials and methods

2.1. Housing and breeding

Wild bank voles (38 males and 54 females) representing the parental generation (P) were caught in August and September on the island Zealand, Denmark, using traditional live traps. The animals were transferred to small barren cages of transparent plastic (13.5 × 16.0 × 22.5 cm) and kept physically isolated in the laboratory under 12 h light conditions (0800–2000 h). The cages were supplied with a woodcutting bed, and food (standard rat chow) and water were available ad libitum. Cage cleaning was performed every second week or when necessary. A portion of a grain mixture was given when the cages were cleaned.

After an initial observation period of at least 5-week duration, single mating pairs were transferred to larger enriched cages (14.5 × 21.5 × 37.5 cm) supplied with a woodcutting bed, toilet paper, and paper rolls. The resultant offspring (F1) consisted of 138 males and 110 females in 52 different litters born from November to May. F1 individuals were weaned between the ages of 25 and 53 days and kept physically isolated for 180 days.

2.2. Observations and classification

One-zero sampling for 3–4 h everyday during the isolation period paid attention to stereotypic behaviour. When stereotypies were recognisable, the age and sex of the voles were noted along with the type of stereotypy performed. Mean daily water consumption was calculated for all animals. No attempts were made to estimate the amount of water not ingested.

Voles were classified as stereotypers (S) if stereotypic behaviour were noted in bouts of at least five repetitions during the daily observation periods. These bouts, separated by small intervals, could continue for hours. The term S covered BS, high-speed jumping (JUMP), PF and WINs as previously defined (Sørensen, 1987; Sørensen and Randrup, 1986; Ödberg, 1986; Cooper and Nicol, 1991, 1996). Voles were classified as polydipsic (PD) if their average daily water intake at least for a continuous month exceeded 21 ml (compared with 10 ml/day for average consumption). Voles showing both PD and S were classified as polydipsic stereotypers (PDS). Voles showing neither PD nor S were classified as wildtype (W).

Twenty polydipsic and 20 non-polydipsic voles were randomly selected and tested for glucosuria as a possible indication of diabetes mellitus (TESTAPE®, Eli Lilly and Company).

2.3. Statistical analyses

Data were tested for normality with Kolmogorov–Smirnov one-sample tests and F-tests for even variances. If data fulfilled the criteria needed for a parametric test, unpaired t-test and one-factor ANOVA were used. If not, data were treated with Kruskal–Wallis tests for general significance, followed by Mann–Whitney U-tests.
Spearman rank correlation tests were used to estimate effects of isolation age on the age of development of stereotypies and polydipsia. Intersex differences in stereotypy frequencies and water consumption were tested with chi-square tests using Yates continuity correction factor. The same test was used on data from polydipsic and non-polydipsic voles with respect to glucosuria. The chosen significance level was 0.05 and the tests were two-tailed. Corrections for ties were performed if necessary.

3. Results

3.1. Stereotypies

Table 1 illustrates the proportion (%) of animals in the four classifications (W, S, PD and PDS) in each of the two generations.

No individuals in the P generation developed stereotypies, whereas stereotypic behaviour was observed in 37% F1 individuals (S + PDS). There were no sex differences in the number of S + PDS animals, but significantly fewer males than females developed stereotypies alone (S) \( P < 0.05 \). Approximately 10% of the F1 animals developed two or more different types of stereotypies. The distribution of different types of stereotypies in F1 is depicted in Fig. 1. The preferred stereotypy was BS \( P < 0.0001 \). JUMP was preferred over PF \( P < 0.01 \) and WIN \( P < 0.0001 \), and no sex differences were shown in stereotypy distribution.

Table 2 shows the age at which the F1 voles were classified as S, PD and PDS. Stereotypies were developed at the age of 96 days for both sexes. Comparisons of the two most common types of stereotypies showed that JUMP appeared earlier (60 days) than BS \( P < 0.0001 \).

There were no relationships between the age at isolation and age at which stereotypies were observed, and there were no effects of isolation age on the number of stereotyping voles.

Table 1

<table>
<thead>
<tr>
<th>Classification/Generation</th>
<th>W</th>
<th>S</th>
<th>PD</th>
<th>PDS</th>
<th>PD + PDS</th>
<th>S + PDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>P (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males (n = 38)</td>
<td>66</td>
<td>0</td>
<td>34</td>
<td>0</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Females (n = 54)</td>
<td>87 *</td>
<td>0</td>
<td>13 *</td>
<td>0</td>
<td>13 *</td>
<td>0</td>
</tr>
<tr>
<td>Males + females</td>
<td>78</td>
<td>0</td>
<td>22</td>
<td>0</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>F1 %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males (n = 138)</td>
<td>38</td>
<td>23</td>
<td>30</td>
<td>9</td>
<td>38</td>
<td>32</td>
</tr>
<tr>
<td>Females (n = 110)</td>
<td>46 *</td>
<td>38 *</td>
<td>11 *</td>
<td>6</td>
<td>16 *</td>
<td>44</td>
</tr>
<tr>
<td>Males + females</td>
<td>42</td>
<td>30</td>
<td>21</td>
<td>7</td>
<td>29</td>
<td>37</td>
</tr>
</tbody>
</table>

* \( P < 0.05 \).
** \( P < 0.001 \).
Fig. 1. Proportions (%) of male and female voles showing different types of stereotypies. The total exceeds 100% because some voles showed two or more stereotypies. Abbreviations as in text.

3.2. Polydipsia

There were no significant differences between the occurrence of polydipsia (PD + PDS) in P (22%) and F1 (29%), but the proportion of polydipsic males was more than twice the proportion of polydipsic females in both generations (P: P < 0.05; F1: P < 0.001) (Table 1). Daily water consumption in male and female W voles was 9.8 and 9.0 ml/day, respectively. S males drank 9.2 ml/day and S females reached 10.3 ml/day (P < 0.05 compared with W females). PD males drank 67.0 ml/day and PD females reached 60.8 ml/day, while PDS males and females drank 65.6 ml/day and 50.7 ml/day, respectively. There was no sex effect on water consumption.

There was no sex difference in age for showing polydipsia, but polydipsia was developed later than stereotypies in males (60 vs. 99 days, P < 0.001) (Table 2). There

<table>
<thead>
<tr>
<th>Day of observation</th>
<th>S</th>
<th>PD</th>
<th>PDS-S</th>
<th>PDS-PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (n = 85)</td>
<td>99</td>
<td>60</td>
<td>86</td>
<td>62</td>
</tr>
<tr>
<td>Females (n = 60)</td>
<td>94</td>
<td>74</td>
<td>90</td>
<td>114**</td>
</tr>
<tr>
<td>Males + females</td>
<td>96</td>
<td>63</td>
<td>87</td>
<td>79</td>
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</table>

<table>
<thead>
<tr>
<th>Day of observation</th>
<th>Males</th>
<th>Females</th>
<th>Males + females</th>
</tr>
</thead>
<tbody>
<tr>
<td>S vs. PD</td>
<td>*</td>
<td>NS</td>
<td>*</td>
</tr>
<tr>
<td>S vs PDS-S</td>
<td>*</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>S vs PDS-PD</td>
<td>*</td>
<td>NS</td>
<td>*</td>
</tr>
<tr>
<td>PD vs. PDS-S</td>
<td>*</td>
<td>NS</td>
<td>*</td>
</tr>
<tr>
<td>PD vs. PDS-PD</td>
<td>NS</td>
<td>*</td>
<td>NS</td>
</tr>
<tr>
<td>PDS-S vs. PDS-PD</td>
<td>*</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

* P < 0.05.
** P < 0.01.
*** P < 0.001.
Table 3

<table>
<thead>
<tr>
<th>Glucosuria %</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polydipsic (n = 20)</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>Non-polydipsic (n = 20)</td>
<td>0 * *</td>
<td>100</td>
</tr>
</tbody>
</table>

* * * P < 0.001.

were no effects of isolation age on the number of voles developing polydipsia, the time for polydipsia to occur or the amount of water consumed.

3.3. Stereotypies and polydipsia

Approximately 7% F1 voles were classified as PDS (Table 1) with no significant difference related to sex.

PDS animals developed polydipsia later (79 days) than PD animals (63 days), and this was especially pronounced in females (114 vs. 74 days, P < 0.05) (Table 2).

Comparisons between all non-stereotyping voles (W + PD, n = 156) and all stereotyping voles (S + PDS, n = 92) showed that polydipsia occurred most frequently in non-stereotypers (W + PD: 34%; S + PDS: 20%, P < 0.05).

3.4. Polydipsia and glucosuria

Table 3 shows the proportion (%) of voles tested positive for glucosuria. None of the non-polydipsic voles were tested positive, whereas 65% polydipsic voles showed clear signs of glucosuria (P < 0.001).

4. Discussion

The present study repeats the previous findings that laboratory-bred, but not wild caught voles, easily develop stereotypies under barren housing conditions (Ödberg, 1986; Sørensen, 1987; Sørensen and Randrup, 1986; Cooper and Nicol, 1991, 1996). Moreover, it demonstrates that males are more disposed to develop stereotypies than females, whereas there are no sex differences in the types of stereotypies shown. BS is the most commonly observed stereotypy in our Danish voles and this is in contrast to the finding of JUMP being the preferred stereotypy in laboratory-bred voles originating from geographically different populations (Sørensen, 1987). Thus, it appears that strain or population differences relate to the types of stereotypies preferably developed in the laboratory. Ödberg (1987) recorded jumping stereotypies before the age of 30 days in voles, and Cooper and Nicol (1991) report that stereotypies in laboratory-bred voles develop when the animals are 4 months old. Apart from possible strain or population differences, estimates of the occurrence of stereotypies depend on the definition of stereotypy employed, and especially on the exact time course (duration and frequency)
that the behaviour has to fulfil in order to be classified as a stereotypy. It cannot be ignored, however, that management and handling of the laboratory-bred voles play a role for the type of stereotypies developed. When cleaning the cages in the present study, it was necessary to transfer the animals from their home cages with old woodcut bedding to cages with new bedding material. During this procedure, young voles responded almost immediately by showing non-stereotyped jumping movements in the cage corners or against the cage walls in both old and new cages. Non-stereotyping older voles responded with digging in the new bedding material while stereotyping voles exhibited their preferred stereotypy. The jumping responses of the young voles occurred in the breeding cages as well as after isolation. Non-stereotyped jumping in young voles may be interpreted as unsuccessful attempts to escape during disturbance, and the lack of a successful outcome of an otherwise adequate escape response could be the source of subsequent stereotypic behaviour (as also suggested by Ödberg, 1986). If so, stereotypic behaviour already developed may be elicited at least partially by the same circumstances that originally caused their development, but in addition that, stereotypies may also occur in other contexts. It could be that these other contexts share the common frustrating feature of unsuccessful results of otherwise adequate behavioural responses such as frustrating effects of social deprivation. The lack of stereotypy development in wild caught voles may thus relate to the lack of such frustrating experiences among young voles in the wild. This interpretation is partially supported by the finding that environmental enrichment of the cage milieu reduces the perseverance of stereotypies in young but not to the same extent in old laboratory-bred voles (Cooper et al., 1996).

The development of spontaneous polydipsia in both wild caught and laboratory-bred voles is difficult to interpret. We assume that polydipsia due to its association with high mortality (Sørensen and Randrup, 1986) is rare in the wild. Polydipsia has been observed as a result of diabetes mellitus induced by prolonged glucocorticoid treatment, exposure to toxins, viral infections, surgical lesions and other presumable stressful influences (Craighead, 1975; Hunt et al., 1976; Mormedes and Rossini, 1981; Schlosser et al., 1984; Tarui et al., 1987; Goodwin, 1991). In the present study, polydipsia was clearly associated with glucosuria. It is therefore possible that keeping voles isolated under barren conditions in the laboratory represents a stressful experience for the animals leading to diabetes and excessive drinking.

Modifying temporal reward patterns under experimental learning conditions can also provoke excessive drinking in rodents (Schedule Induced Polydipsia or SIP) and this experimentally induced response is frequently used as an animal model for human mental disorders (e.g. Woods et al., 1993; Roehr et al., 1995). Polydipsia is a characteristic feature of chronic schizophrenic humans, but although some psychopharmacca effectively reduce spontaneous polydipsia in psychiatric patients (Fuller et al., 1996; Spears et al., 1996; Verghese et al., 1996), provoked SIP in rodents may be left unaffected by similar treatments (Roehr et al., 1995). Referring to the above-mentioned possible frustrating or stress-related feature of keeping voles isolated under barren conditions, the occurrence of polydipsia in the present study may very well parallel the condition of SIP, which also seems associated with frustration.

Combinations of causes may also explain polydipsia development, but the validity of the interpretations presented here will have to await further and more specific studies.
The same holds true for explaining why males seem more prone to develop polydipsia than females, while no major sex differences were found in the tendency to develop stereotypies. One possibility is, of course, that both sexes experience frustration under the laboratory conditions leading to stereotypies, but that males are more easily brought to a state of prolonged stress, and for that reason, more easily develop the pathologic state of polydipsia and perhaps diabetes mellitus. Based on the present findings, the development of stereotypies appears to mitigate the development of polydipsia in both sexes. Very few individuals developed both stereotypies and polydipsia, but among these few, polydipsia occurred later than in voles developing polydipsia alone.

In conclusion, we suggest that the development of stereotypies and polydipsia among bank voles in the laboratory are the results of frustration and prolonged stress. Stereotypies seem to depend on frustrative experiences early in life, while polydipsia may be related to diabetes mellitus caused by the experience of prolonged stress. Moreover, circumstances related to the development of stereotypies may have an adaptive value by reducing the risks of prolonged stress, including the development of fatal polydipsia.

Acknowledgements

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References


