Research report

Isolation rearing affects sequential organization of motor behavior in post-pubertal but not pre-pubertal Lister and Sprague–Dawley rats

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Abstract

Objective: Dopaminergic and serotonergic modulation potently influences the sequential organization of rat movements in a simple unconditioned motor paradigm. Rats reared in social isolation post-weaning differ profoundly from their socially reared litter mates on behavioral, neurochemical, and neuroanatomical measures. This investigation examined (1) whether social isolation significantly affects the sequential organization of rat movements, (2) whether these changes occur at different ages, and (3) whether these changes differ across strains. Method: male Lister and Sprague–Dawley rats reared in isolation post-weaning and socially reared controls were tested at 2 and 8 weeks post-weaning, in the Behavioral Pattern Monitor for 30-min sessions. The amount of activity and the spatial patterns of movements as measured by both the spatial scaling exponent and the fluctuation spectrum of local spatial scaling exponents were assessed in 10-min intervals. Results: Habituation of locomotor activity was significantly attenuated in isolation reared rats during the 30-min sessions irrespective of strain. Spatial patterns of movements were significantly affected by isolation rearing in movements in post-pubertal but not pre-pubertal Lister and Sprague–Dawley rats. The spatial scaling exponent and the fluctuation spectrum analysis revealed a shift towards straight, distance-covering, and repetitive movements rather than a complex re-organization of the behavioral repertoire. Conclusions: Isolation rearing profoundly affects the sequential organization of movements in post-pubertal rats, suggesting that emerging behavioral dysfunctions parallel developmentally those found in patients with schizophrenia. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

Rats reared in social isolation post-weaning (isolates) exhibit profound behavioral, neurobiological, and neuroanatomical differences when compared to their socially reared litter mates (socials). Isolates relative to socials were found to be hyper-reactive in novel environments (e.g. [10]), exhibited slower rates of habituation of locomotor activity [7], and were more aggressive [3], did not show preferences for novel foods under novelty conditions [13], and are more sensitive to the stereotypy effects of direct and indirect dopaminergic agonists [24]. In a previous study of Lister rats, 8 weeks of isolation rearing lead to an increase in spontaneous locomotor activity, deficits in prepulse inhibition of the acoustic startle response which were reversed by the dopamine (DA) antagonist raclopride, and no effect on latent inhibition in a conditioned suppression paradigm. These changes were accompanied by an en-
enhanced basal and D-amphetamine stimulated DA release in the ventral striatum, as measured by in vivo microdialysis [26]. Thus, isolates exhibit neurochemical and behavioral abnormalities suggestive of hyperactivity in mesolimbic DA systems. Moreover, it has been suggested that isolation rearing provides a non-pharmacological manipulation to induce sensorimotor gating deficits in rats similar to the information processing deficit observed in schizophrenia patients [9].

In learning paradigms, isolates reached performance accuracy comparable to that of socials, however, these animals were found to make more errors during the acquisition of a conditional discrimination task. In contrast, the discrimination performance in isolates was less disruptable by manipulations of the task requirements when compared to socials and performance in isolates was found to be remarkably resistant to changes in motivational variables. Finally, isolates responded more frequently during conditions of extinction and were virtually unaffected by pre-feeding prior to testing. These findings have been suggestive of a rigid behavioral repertoire in isolates which exhibits more resistance to change with respect to paradigmatic manipulations, learning, and extinction. These suggestions are further confirmed by the fact that isolates exhibited stronger position habits than socials following reversal of the contingencies and suggest a specific impairment in rule learning in these animals [15].

The effects of social isolation have been linked neurochemically to dysfunctions of the DA system. Firstly, treatment with DA receptor D1 or D2 antagonists enhanced the rate of response to intra-accumbens D-amphetamine in socials but not isolates [21]. Secondly, isolates were more active in a novel environment, and were more responsive to the locomotor stimulant action of cocaine. Thirdly, in drug discrimination studies, isolates acquired a selective response on the drug lever at lower doses than socials. Isolation rearing shifted the cocaine dose-response function to the right and impaired the selectivity of the response on the drug lever at lower doses of cocaine. Fourthly, in the absence of cocaine, the contingent presentation of the conditioned reinforcer enhanced selectively the rate of response by socials but not by isolates [22]. Fifthly, isolates showed an altered time course of locomotor activity following D-amphetamine sulphate administration and an increased sensitivity to the sedative effects of a low dose of apomorphine but did not differ from socials following higher doses of the drug. Sixthly, isolates were found to exhibit more stereotypy in a low-aversive environment when injected with low doses of apomorphine or amphetamine [24]. Finally, isolates showed greater increases in extracellular DA and greater decreases in DOPAC in response to 2 mg/kg amphetamine. However, isolation rearing did not affect cAMP accumulation in response to stimulation of D1 DA receptors by DA. Thus, isolation rearing did not affect the coupling between D1 and D2 receptors.

Alternatively, serotonergic systems have been implicated in the mediation of the isolation induced behavioral changes. For example, behavioral studies using forepaw treading and flat body posture which are thought to be mediated by 5-HT1A receptor activation, and stimulation of this receptor by either 5-MeODMT or 8-OH-DPAT produced greater responding in isolates suggesting supersensitivity of the post-synaptic 5-HT1A receptor. Moreover, increased wet-dog shakes and back muscle contractions which are thought to be mediated by 5-HT2 and other (none-5-HT) receptors suggest that there appears to be an increase in 5-HT2 receptor responsiveness in the isolates [28]. These findings are substantiated by the observation that isolates were found to have a lower 5-hydroxyindoleacetic acid (5-HIAA)/5-hydroxytryptamine (5-HT) ratio and a reduced basal perfusate concentration of 5-HIAA in the nucleus accumbens [14]. Taken together, these neurochemical changes suggest a complex dysregulation of both dopamine and serotonin in areas that are crucially involved in response generation, selection, and sequencing.

Unconditioned motor activity consists of a wide variety of behavioral responses that can be quantified by measures assessing distinct dimensions of behavior. Previous investigations have shown that the amount of motor activity is only one aspect of the behavioral repertoire. In addition, sequential organization of behavioral elements and investigatory responses have emerged as independent dimensions of unconditioned motor behavior [18]. Moreover, pharmacological manipulations of both dopaminergic and serotonergic systems have revealed that the sequential organization of behavior is crucially dependent on a regulated interaction of both systems [19]. Specifically, both indirect DA agonists and 5-HT releasers increase the amount of activity but affect the organization of movements in opposite ways. While low doses of amphetamine treatment result in a randomized movement pattern, 5-HT releasers such as the substituted methamphetamines MBDB or MDMA lead to highly repetitive straight movement patterns. Thus, assessing the effects of social isolation on sequences of behavior will clarify the role of these systems. Moreover, recent investigations of early neurobiological manipulations have revealed that some behavioral effects emerge only after puberty [16]. These findings have been taken to suggest a developmental similarity with some human mental disorders such as schizophrenia [25]. Social isolation affects the neural systems of the rat at a critical time in development. Moreover, prepulse inhibition deficits emerge
after puberty in isolates (unpublished data). Therefore, to determine whether changes in sequential organization of behavior parallel those changes observed in prepulse inhibition, the effect on social isolation on sequential organization of behavior was investigated before and after puberty.

Three specific hypotheses were tested in this study. Firstly, it has been suggested that locomotor activity and habituation are crucial parameters when determining the degree of assimilation to a novel environment [1]. Moreover, variable effects on motor behavior have been reported for rats reared in social isolation based on the degree of novelty to the testing environment. For example, when tested in novel situations, in contrast to their enhanced motor activity, isolates have shown reduced exploration and orienting [6]. While some groups have reported no change in habituation [6], others suggest that individually housed rats were hyper-reactive in novel environments and showed a slower habituation at all time points tested [7]. Finally, in a previous study, isolation rearing was found to increase locomotor activity in Lister but not Sprague–Dawley rats [9]. Therefore, it was hypothesized that social isolation rearing results in a strain-specific increase of locomotor activity and an attenuation of habituation.

Secondly, based on the profound effects of social isolation rearing on both DA and 5-HT systems [2], a proposed rigidity of the behavioral repertoire, and the similarity between sensory gating dysfunctions in the animals and those found in schizophrenia patients, it was hypothesized that social isolation rearing significantly affects sequential organization of behavior as measured by the spatial scaling exponent, $d$. This measure quantifies the geometric characteristics of movement sequences and sensitively measures stereotypic movements. Repetitive behavioral sequences can result in both straight movements as observed with 5-HT releasers and some agonists [19] as well as highly circumscribed movements, such as those generated by high doses of amphetamine or other indirect DA agonists [20]. Thus, an increase in straight movements may indicate a dysregulation of the serotonergic system whereas an increase in circumscribed movements may point toward a dopaminergic dysregulation.

Thirdly, based on previous findings suggesting that sensory gating deficits parallel those found in schizophrenia patients and recent results indicating a complex dysregulation of behavioral organization in schizophrenia patients, it was hypothesized that the deficit in sequential organization of behavior emerges significantly only after puberty. Thus, animals reared in social isolation were examined at age 35 days and age 85 days, i.e. substantially before and after the onset of puberty.

2. Methods

Four separate experiments were conducted. For each experiment, rats were exposed only once to the apparatus, testing was performed during the animals’ dark-cycle or high activity period. For two experiments, Lister rats (Harlan, UK) weighing 250–300 g were used, for the other two experiments, Sprague–Dawley rats weighing 250–300 g (Harlan, San Diego, CA) were used. For each experiment, animals were received 1 day after weaning (day 21) and were subsequently housed singly in metal cages or housed in groups of three animals. Those animals which were housed singly were able to hear, see, and smell the other animals but did not have any physical contact with other rats. Handling was kept at a minimum and restricted to regular health checks and bedding changes.

To test the hypotheses outlined above, two groups of animals, i.e. Lister and Sprague–Dawley rats were either reared socially or kept in social isolation for 2 or 8 weeks post-weaning. Therefore, results are reported on eight different groups: socially reared Lister or Sprague–Dawley rats at 2 weeks post weaning (Lsoc2, SDsoc2); isolation-reared Lister or Sprague–Dawley rats at 2 weeks post weaning (Liso2, SDiso2); socially reared Lister or Sprague–Dawley rats at 8 weeks post-weaning (Lsoc8, SDsoc8); isolation-reared Lister or Sprague–Dawley rats at 8 weeks post-weaning (Liso8, SDiso8). These durations were selected to determine pre-pubertal and post-pubertal isolation effects.

2.1. Apparatus and testing

Following the different rearing periods, animals were brought to the laboratory prior to testing in the Behavioral Pattern Monitor (BPM). Each testing session lasted 30 min. The BPM has been described extensively in [8] and consists of eight black chambers, each enclosed within a ventilated wooden box. Each chamber consists of a 30.5 x 61.0 x 38.0 cm Plexiglas holeboard equipped with three floor holes in the front, middle, and rear part of the floor, six wall holes, three along either side of the long walls, and a hole in the back of each chamber. The location of the rats in the BPM chambers was obtained from a grid of 4 x 8 photo-beams 2 cm above the floor in each chamber. The information about the status of the photobeams and the touchplate was transmitted with a frequency of 18 Hz to a PC-compatible computer. Whenever a change in the status of photobeams occurred, the information was stored in data files together with the duration of the photobeam status. Subsequently, the raw data files were transformed into ASCII data files consisting of the $(x,y)$ location of the rat in the BPM chamber with a resolution of 3.8 cm, yielding $7 \times 15$ different possible positions and the duration of each event ($t$). Thus, the
data set is comprised of sequences of micro-events defined by distinct coordinates consisting of \((x, y, t)\).

2.2. Behavioral assessment

The behavioral assessment for the different experimental groups is based on the sequences of micro-events. Simple descriptors of the motor activity were obtained from the sequences of micro-events. The counts of \((x, y, t)\) quantifies the amount of activity and comprises all micro-events within a specified period of time. In addition, hole pokes were counted during a specified period of time to assess exploratory activity. We have previously proposed a scaling hypothesis [18] for the quantitative assessment of spatial patterns of movement sequences. This hypothesis relates the distance traveled between \(k\) micro-events to the number, \(k\), of distinct micro-events. Thereby, straight movement sequences can be differentiated quantitatively from circumscribed movement sequences. Specifically, a linear relationship between distance traveled and the number of micro-events is characteristic for straight movements, i.e. the distance between four micro-events is less than twice as large as the distance between two micro-events. In contrast, a nonlinear relationship between distance traveled and the number of micro-events is characteristic for circumscribed movements, i.e. the distance between four micro-events is less than twice as large as the distance between two micro-events.

The particular functional form relating the distance traveled to the number of micro-events is derived from scaling approaches in physical systems, which have yielded a remarkable universality [5], as well as from the description of a geometrical object using its fractal dimension [17]. This functional form as applied to the pattern analysis of movements reads as follows:

\[
\text{[distance traveled]} (\text{[between } k \text{ micro }- \text{events]}) \\
\approx m^{\text{scaling exponent}} \text{[distance traveled]} \\
\text{[between } m \times k \text{ micro }- \text{events]}
\]

The scaling relationship is described quantitatively by the spatial scaling exponent, \(d\).

The fluctuation spectrum of local spatial scaling exponents, \(f(d)\), is used to quantify the frequency of movements characterized by straight patterns or \(d \approx 1\) and circumscribed patterns or \(d \approx 2.0\) [20,23]. Briefly, this function quantifies how frequently distances between micro-events are observed on different levels of resolution and is based on the following formulation

\[
\text{[Number of]} \\
\text{(local scaling exponent, } d, \text{ between } k \text{ micro }- \text{events}) \\
\approx k^{f(d)}
\]

For the analysis of rat movements, the Euclidean distance between two micro-events is calculated for different segments at different levels of resolution, \(k\). In addition, the distances for different \(k\) are averaged within each segment to improve the estimation of \(d\).

Based on results from previous studies [18], the segment size was set at 16 micro-events and the resolution range, \(k = 1 \text{ to } 12\). In addition, the contribution of artifactually small distances due to the lower resolution limit of the recording instrument is reduced by ‘data dithering’ [18]. The details of the calculation of the fluctuation spectrum of local spatial scaling exponents is described in [20]. The fluctuation spectrum was averaged across rats within each group and the differences between the functions were assessed using a \(t\)-score difference function as detailed in [20].

2.3. Statistical comparisons

Based on the hypotheses advanced above, a multiple analysis of variance (ANOVA) was computed from the scores of the different groups. Specifically, a three between (strain, isolation status, pre/post puberty) and one within ANOVA (time in enclosure) was calculated and Greenhouse Geisser (GG) adjustment of degrees of freedom was applied for the within subjects results. All effects are described in the results section with their associated significance level and degrees of freedom. The calculations were performed using the BMDP 4v software [29].

3. Effects of social isolation on overall assessment of unconditioned motor activity

3.1. Levels of locomotor activity: counts

As shown in Fig. 1 and Fig. 2, male Lister rats were significantly less active during the 30 min exposure in the BPM when compared to Sprague–Dawley rats \((F_{(1,139)} = 78.12, \; P < 0.001)\). Moreover, both strains exhibited a significant increase in locomotor activity at 8 weeks post-weaning when compared to 2 weeks post-weaning \((F_{(1,139)} = 84.23, \; P < 0.001)\). However, this increase was less pronounced for Lister rats when compared to Sprague–Dawley animals \((F_{(1,139)} = 8.6, \; P < 0.01)\). Social isolation did not have an overall effect on the amount of activity, \((F_{(1,139)} = 0.68, \; \text{NS})\). However, there was a slight increase at 2 weeks post-weaning, and a slight decrease at 8 weeks post-weaning, resulting in a significant interaction between age and isolation rearing \((F_{(1,139)} = 4.00, \; P < 0.05)\).

As expected, the amount of activity habituated significantly during the 30-min exposure in the BPM \((F_{\text{GG}(1.69,234.45)} = 578.77, \; P < 0.001)\). This habituation was more pronounced for rats 8 weeks post-weaning.
compared to those 2 weeks post weaning, \( F_{GG(1.69,234.45)} = 21.44, P < 0.001 \). Moreover, this habituation was less pronounced for Lister compared to Sprague–Dawley rats \( F_{GG(1.69,234.45)} = 27.60, P < 0.001 \). Social isolation significantly reduced habituation irrespective of strain \( F_{GG(1.69,234.45)} = 21.54, P < 0.001 \).

Thus, both strain and age exert strong effects on the amount and habituation of motor activity. However, the habituation curves are significantly altered by social isolation rearing. Thus, it is not surprising that variable results have been reported for social isolation rearing with respect to the amount of motor activity [7,6]. These results suggest that longer behavioral test sessions that are more significantly affected by habituation should result in more significant differences in levels of locomotor activity between socially and isolation-reared animals.

4. Overall behavioral organization: spatial scaling exponent \( d \)

As shown in Fig. 3 and Fig. 4, both Lister and Sprague–Dawley rats exhibited similar patterns of movements as measured by the spatial scaling exponent, \( d (F_{(1,139)} = 2.23, \text{NS}) \). The overall mean for \( d \) \( (1.532 \pm 0.004) \) indicates that both groups of animals engage, on the average, in a meandering pattern that is characterized by an equilibrium between straight and circumscribed movement. However, the patterns of movement were significantly affected by age in both groups \( (F_{(1,139)} = 207.34, P < 0.001) \), indicating that
older animals engage in relatively more circumscribed movements. Isolation rearing had a significant effect on these movement patterns, \( (F_{1,139} = 11.16, \ P < 0.001) \) indicating that isolation-reared animals made more straight movements compared to their socially reared controls. However, this effect was only significant for the animals 8 weeks post-weaning as opposed to those 2 weeks post-weaning as indicated by the significant interaction between age and isolation, \( (F_{1,139} = 6.86, \ P < 0.01) \).

Exposure time in the BPM significantly affected the spatial scaling exponent \( d \) \( (F_{GG(1.32,183.34)} = 40.99, \ P < 0.001) \) suggesting that with habituation, i.e. reduction of the amount of motor activity, animals engage in significantly more circumscribed movements as indicated by the overall \( d \) measure for the first 10 min \( (d = 1.4995 \pm 0.0069) \) when compared to the last 10 min \( (d = 1.5725 \pm 0.0104) \). This effect was slightly more pronounced for the Lister when compared to the Sprague–Dawley animals \( (F_{GG(1.32,183.34)} = 5.39, \ P < 0.05) \).

However, time spent in the BPM did not have a differential effect on the sequential organization of movements in socially or isolation-reared animals, irrespective of strain \( (F_{GG(1.32,183.34)} = 3.42, \ NS) \) or age \( (F_{GG(1.32,183.34)} = 2.00, \ NS) \).

Thus, geometric patterns of movements were affected significantly by isolation rearing with isolates exhibiting more straight movement patterns which are more predictable and more strongly correlated. Interestingly, this effect emerged in both strains only at 8 weeks post-weaning, and was not seen at 2 weeks post-weaning.

5. Detailed assessment of behavioral organization: fluctuation spectrum of local spatial scaling exponents, \( f(d) \)

The fluctuation spectrum of local spatial scaling exponents, \( f(d) \), which quantifies the contribution of movements with different geometric properties to the average spatial scaling exponent, was examined for both Lister and Sprague–Dawley animals for the 2 and 8 week post-weaning groups. Differential changes in the repertoire of movements can be detected using this function [20]. Moreover, this function allows one to determine whether the change in the spatial scaling exponent at post-weaning week 8 resulted from a simple shift or a more complex re-organization of movements.

The \( t \)-difference score functions between socially and isolation-reared animals are shown in Fig. 5 and Fig. 6 for the first 10 min block of the 2 and 8 week post-weaning groups, respectively. These difference functions indicate that at 2 weeks post-weaning, Lister isolates engage in significantly more circumscribed movements and fewer straight movements when compared to so-
sials. While Sprague–Dawley isolates do not differ significantly from Sprague–Dawley socials at 2 weeks, there is a trend for an increase in straight movements and a decrease in circumscribed movements in Sprague–Dawley isolates relative to Sprague–Dawley socials. At 8 weeks post-weaning, both Lister and Sprague–Dawley isolates relative to their respective socially reared controls engage in fewer circumscribed movements and more straight movements. Thus, while the fluctuation spectrum provides a more detailed quantitative assessment of the contributions of movement sequences with different geometric characteristics, the average spatial scaling exponent, $d$, completely captures the isolation induced changes. Consequently, for both Lister and Sprague–Dawley rats isolation rearing at 8 weeks post-weaning results in a simple shift towards more straight movements rather than a complex reorganization of the behavioral repertoire.

6. Discussion

There are three main findings of this investigation. Firstly, social isolation rearing, while not increasing the overall amount of motor activity, attenuates significantly the habituation of locomotor activity to this novel environment for both pre- and post-pubertal Lister and Sprague–Dawley rats. Secondly, social isolation rearing significantly increased straight movement sequences for post-pubertal but not pre-pubertal Lister and Sprague–Dawley rats. Thirdly, the changes in the geometric characteristics of movements are sufficiently described by an overall shift toward straight and more predictable movement sequences as opposed to a complex re-organization of the behavioral repertoire of movements.

The results could not confirm the first part of the first hypothesis that isolation rearing results in a strain-specific increase of locomotor activity. However, the results supported the second part of the first hypothesis that isolation attenuates habituation of locomotor activity. In agreement with previous studies [4] [6], both pre- and post-pubertal isolate Lister and Sprague–Dawley rats exhibited significantly attenuated habituation of locomotor activity. Moreover, Hall et al. [12] have shown recently that isolates exhibit significantly increased locomotor activity only during the second 30-min interval in a low-stress environment. There are several possible explanations for the lack of an overall effect on levels of motor activity. Firstly, these animals were tested during their active phase, yielding a high baseline of motor activity. Secondly, the BPM is able to record even small movements which contribute significantly to the overall measure of activity. Thirdly, since the patterns of movements of isolates differ significantly from those of socials in that these animals engage in long straight movements, it is conceivable that a coarser grid of photo-beams would easily detect an increased level of motor activity in the isolates. However, the detailed recording of motor movements allows one to distinguish between levels of motor activity, patterns of motor activity, and habituation effects. The results of these experiments clearly indicate a significant effect of isolation rearing on the latter two.

This investigation confirmed the second hypothesis that isolates and socials differ in their patterns of movements. The effect size of the increase in straight movements was similar for both Lister and Sprague–Dawley rats. However, this difference was only significant in animals that have been reared in social isolation for 8 weeks post-weaning, i.e. post-pubertal rats. An increase in straight movements and a corresponding decrease in circumscribed movements, as indicated by the fluctuation spectrum of local scaling exponents, $f(d)$, in these animals indicates an overall shift of the behavioral repertoire towards straight movements. Movement patterns with different geometrical characteristics are thought to serve different functions in the unconditioned motor paradigm. Specifically, a combination of straight and circumscribed movements is necessary to engage in both varied and local exploration of the novel environment [8]. It has long been proposed that the direct contact with external stimuli serves to decrease the novelty of the environment and furthers the habituation of the animal’s behavior [1].
The ‘dissociation’ of the frequency of straight movement from that of circumscribed movements may also help to explain the complex interaction between novelty, arousal, and primary rewarding stimuli reported in [10–12]. Specifically, isolates compared to socials exhibited less differential responding when approaching novel versus familiar foods in a novel environment, however, did not show differences in consummatory behavior or exploration of a novel environment. Moreover, isolates were more sensitive to the contrast enhancing modulation of primary rewarding stimuli. Finally, isolates were found to have a greater preference for novel environments in a low-aversive environment. Taken together, these results suggest that isolates are more sensitively influenced by incentive stimuli, however, exhibit less differential responding when approaching novel environments or rewarding stimuli. In the BPM, these behavioral changes translate to an increased tendency to move to a different part of the enclosure without a differential exploration of the area. Said differently, isolates are ‘driven’ to a novel area of the BPM without exploring the area in detail. Future studies may test the hypothesis whether ‘the lack of detailed exploration’ in isolates characterized by decreased circumscribed movements is directly related to a decrease in habituation to a novel environment.

In addition to the heuristic explanatory concept of exploration, the changes in patterns of movements can also be seen in terms of adaptability, predictability, and rigidity of the behavioral repertoire. Specifically, the significant reduction in $d$ corresponding to increased straight movement sequences also represents an increased predictability of the movement sequences. This increase in correlation or predictability between individual behavioral elements in isolates is consistent with the interpretation that the sequence is less susceptible to external influences. In other words, the next movement of the animal is more strongly predicted by the previous movement and is to a lesser extent an adaptive response to the environmental stimulus, i.e. the enclosure. This finding is congruent with those of others who have reported an increased sensitivity to stereotypy induced by both direct and indirect DAergic agonists [24]. Moreover, the shift of the repertoire of movements towards more strongly correlated movements as indicated by the $f(d)$ function further supports the notion of a more restricted behavioral repertoire. This finding, therefore, confirms the reports by others [15] that isolates, while able to learn, show higher error rates, more resistance to extinction, and are less susceptible to paradigmatic and motivational manipulations. Moreover, the finding of increased straight movement sequences in isolates is not incompatible with recent reports showing enhanced learning in the water maze paradigm [27]. Specifically, quickly locating a hidden platform in a relatively large water tank may be facilitated by repetitive straight, distance-covering movement sequences. Thus, the assessment of the sequential organization of movements using this simple unconditioned motor paradigm can provide significant information beyond the assessment of the amount of activity. Specifically, the sequential processes that are thought to underlie the changes in the behavioral repertoire induced by isolation rearing can be studied in a simple behavioral paradigm that are otherwise elucidated in much more complex behavioral paradigms.

The results of this investigation also confirmed the third hypothesis that differences in sequential organization of motor behavior between socials and isolates emerge in post-pubertal animals. Specifically, for both Lister and Sprague-Dawley rats, social isolation resulted in patterns of movements that are significantly more straight and correlated after 8 weeks of isolation but not 2 weeks of isolation. In addition, this emerging difference was disassociated from changes in the amount and/or habituation of locomotor activity. This differential effect of isolation rearing on movement sequences suggests that these changes may be mediated by different neural substrates. In particular, 5-HT reuptake inhibitors as opposed to DA releasers result in movement sequences with geometric characteristics not unlike those observed in isolates [18]. While there is clear evidence that the DA system plays a crucial role in the mediation of the behavioral effects induced by isolation rearing [21] [22], this investigation provides data for a novel hypothesis. Specifically, future studies will examine whether the sequential organization of movements as opposed to the amount and habituation of movements are selectively mediated by the 5-HT system. This hypothesis would provide a crucial link in the same behavioral paradigm between the proposed DAergic and 5-HTergic dysfunctions that have been studied by others in a variety of different behavioral paradigms [15,27,28].

The confound between age and duration of isolation is a significant limitation of this experimental series that cannot be directly resolved using this experimental design. There are several arguments that can help to disentangle these factors. Firstly, early investigations have shown that the effects of social isolation on object contact in an open-field are critically dependent on the time but not the duration of isolation [4]. Specifically, whereas isolation between 25 and 45 days of age produced an irreversible effect upon object contact, neither isolation between 16 and 25 days or after 45 days resulted in this effect. Thus, even extended isolation during adulthood does not produce these changes in behavior. Therefore, it is unlikely that the duration of isolation instead of age at time of testing had a significant effect on motor behavior. Secondly, the detailed assessment of the changes in movement sequences using the fluctuation spectrum analysis indicates that even...
After 2 weeks of social isolation Sprague–Dawley but not Lister rats exhibit changes in patterns of movements similar to those found in post-pubertal animals. Thirdly, patterns of movements change significantly across different ages of rats. Specifically, circumscribed movements significantly increase with age. Thus, compared to the movement patterns of socials, isolates engage in movements that are more like those of younger animals suggesting that there may be a significant retardation of development of movement patterns that are used to explore a novel environment. To summarize, there is evidence from other experiments [4] to suggest that social isolation rearing results in a developmentally specific effect in rats. In these experiments, the effect on patterns of motor behavior was evident post-pubertally but not pre-pubertally. Other experiments show that post-pubertal isolation does not result in behavioral changes characteristic of post-weaning social isolation. Together, these results suggest that the expression of the behavioral deficit induced by isolation rearing is found after a developmental delay and is, therefore, not unlike some of the pathological processes suggested to account for the deficit in schizophrenia [9].

In summary, social isolation significantly affects unconditioned motor behavior in several distinct ways. Firstly, a lack of habituation is already evident in pre-pubertal animals. Secondly, movement pattern changes emerge in post-pubertal animals. Thirdly, the overall behavioral repertoire is shifted towards more predictable and less adaptive behavioral sequences. These behavioral changes are not unlike those observed in behavioral paradigms with schizophrenia patients. Therefore, further investigations are indicated to better elucidate the neural substrate and behavioral correlates of social isolation rearing as a possible behavioral model for some behavioral deficits observed in schizophrenia.

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