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Comparison of Haloperidol- Versus Phenazepam- Induced Anxiolytic Effect on Rodent Behavior

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Abstract. This study investigated the effects of phenazepam and haloperidol, recognized as a tranquilizer and an antipsychotic, respectively, on anxiety using the open field test. We employed conventional behavioral assessments alongside color-tracing and color-coding methodologies to examine the comparative influences of two chosen drugs. Both compounds induced a reduction in locomotor activity, though with nuanced differences. Phenazepam's suppressive effect manifested later, countered by increased traverses along the periphery, while haloperidol's impact was evident earlier, accompanied by localized movements. Analysis of movement initiation revealed distinct patterns between the groups, suggesting phenazepam's influence on cortical processes and haloperidol's Impact on anxiety-related behavior. Despite reduced central exploration, interpretation of anxiety levels necessitates consideration of drug effects and environmental context. Our findings underscore the complexity of assessing anxiety solely based on motor activity, emphasizing the importance of incorporating emotional dimensions in clinical evaluations. This nuanced understanding is vital for optimizing therapeutic interventions in psychiatric care.

Keywords: Open Field Test · Phenazepam · Haloperidol · Behavior · Color-Coding · Color-Tracing

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1 Introduction

The behavior of patients associated with excitement, tension, and unreasonable fear can put their life and health in danger due to possible self-injury or other destructive manifestations. In such cases, the use of antipsychotics and/or anxiolytics is practiced, the most common of which are haloperidol or anxiolytics tranquilizers from the benzodiazepine family, for example, phenazepam [1–5]. These drugs also affect the behavior of animals. In particular, it has been confirmed that haloperidol helps correct stress behavior in rodents and birds [6]. Haloperidol is a butyrophenone derivative. Butyrophenones are typical antipsychotic drugs indicated to patients with positive symptoms such as delusions, mania, psychosis, disorganized thinking. The mechanism of action is still not fully understood but the drugs are assumed to have an inhibitory effect on the ascending pathways from the reticular formation, associated with blocking D2 dopamine receptors (DR) [7–10] in the mesolimbic pathway. The side effects include extrapyramidal symptoms, provided by the nigrostriatal pathway receptors [11]. In addition to antagonizing D2 DR, haloperidol also reveals activity against an additional range of G protein-coupled receptors (GPCR) in the central nervous system, including other DR subtypes, serotonin (5-HT2) receptors and α-adrenoceptors [12–14]. Haloperidol-injection rodents are often used as a model to study pharmacologic treatment of extrapyramidal disorders [15, 16]. The development of animal models of anxiety is often based on their sensitivity to anxiolytic drugs [17], an example of which is phenazepam, a member of the 1,4-benzodiazepine group, along with diazepam, nordazepam, oxazepam, and temazepam. Benzodiazepines interact with GABAA ionotropic receptors, increasing their affinity for the mediator gamma-aminobutyric acid (GABA) and increasing the flow of chloride ions into neurons, thereby reducing their excitability. Benzodiazepine-sensitive GABAergic receptors are widely distributed in the brain [18] but the main neurological areas of involvement are primarily the amygdala and reticular activating system [19]. Phenazepam was developed in the 1970s to treat epilepsy, withdrawal symptoms, insomnia, anxiety, and as a drug that inhibits reflexes in several areas of the brain and spinal cord [20, 21]. From a pharmacological point of view, phenazepam is several times more active than diazepam, but has more severe and persistent side effects, including amnesia, drowsiness, dizziness, muscle weakness, decreased concentration and attention, im-paired coordination, blurred speech, etc. [22]. Its use in animal behavior tests can be considered as a model for anxiety treatment in humans. Tranquilizers such as phenazepam or diazepam expectedly reduce locomotor activity due interaction with benzodiazepine-sensitive site on GABAA receptor, binding to which makes GABAergic transmission more efficient and leads to an anxiolytic or sedative effect, depending on the emotional state of the animals [23, 24]. A comparative analysis of the sedative and anxiolytic effects of antipsychotic drugs versus tranquilizers of the benzodiazepine family has been carried out mainly in pa-tients and quite rarely on behaving rodents. Thus, in an early study, haloperidol was shown to be more effective than diazepam in treating symptoms of fear and anxiety [25]. Haloperidol could not only provide greater relief for patients, but also produced fewer side effects. In a more recent study, the extensive data accumulated on patients have been summarized [26], with an overall conclusion that haloperidol, and not benzodiazepines, should be considered as a first-line drug for the treatment of agitated states. A report by Ulaka et al. [27] also concluded that haloperidol, compared with diazepam, has a greater anxiolytic effect and reduces pain. Comparative alternations of motor behaviors in rodents under the influence of antipsychotics and tranquilizers have not been specifically studied. In all very few cases known to us, compari-sons were made on certain genetic models and/or under specific pharmacological contexts. For example, one study examining stereotypical motor activity in rats under the influence of amphetamine found that haloperidol blocked the effect of amphetamine on stereotypic behavior and increased motor activity, whereas diazepam did not affect the level of horizontal motor activity [28]. Another study has shown that haloperidol restricts horizontal locomotor activity, while diazepam is more anxiolytic, increasing the overall activity and time spent in the center of an open field in mice. [29]. Thus, the scarce literature data creates a somewhat contradictory picture of the anxiolytic effect of haloperidol compared to drugs from the benzodiazepine group. However, such data may have significant implications for both theory and clinical practice. The most adequate platform for such testing seems to be the open field (OF) setup. The OF test is widely used to study the behavior and general activity of rodents [30]. It provides a simple and relatively quick assessment of behavior without requiring complex training [31]. For the animal, it provides a sense of open space in the center of the arena [32]. The application of the test makes it possible to investigate a number of dynamic factors that consist of the general motor activity and behavioral features: locomotion, freezing, exploration, sniffing, rearing, grooming, etc. [33, 34]. Testing begins with placing the rodent in the peripheral or central part of the field [35]. To quantify movements, the arena is usually divided into visible or invisible equal sectors [36–39]. The rodent placed in the OF, initially may keep close to the walls. As it becomes accustomed, the animal begins exploring the central areas, making runs and stands. More anxious animals spend significantly less time in the central sectors, continuing to stick to the periphery. In addition, manifestations of fear are indicated by frequent defecation and freezing [40, 41]. In the proposed study, we compare the dynamic effect of haloperidol and phenazepam potentially able to affect anxiety in the OF. We use several novel approaches, such as spatial and temporal color coding, which allow efficient and high-resolution estimation of dynamic behavior patterns [42–44].

2 Materials and Methods

The study was conducted in accordance with the principles of the Basel Declaration, the Order of the Ministry of Health of the Russian Federation of April 1, 2016 No. 199n “On Approval of the Rules for Good Laboratory Practice” and the recommendations of the Bioethical Commission of Saint-Petersburg Chemical State University of the Russian Ministry of Health. The vivarium was maintained at a constant temperature of 24 °C, the humidity level in the room was kept within the standard range. Animals received a regular, balanced diet. The day/night cycle was 12/12 h.

The series of experiments was carried out on 30 outbred rats, divided into 3 groups in accordance with the administered drug. The rats of the control group were injected with a saline solution at a volume of 0.5 ml. Phenazepam (Novosibkhimfarm pharmaceutics company), was diluted in physiological solution and administered at the concentration of 1 mg/kg. The dose of haloperidol (Gedeon Richter, Hungary) was 0.3 mg/kg. The exposure time after drug administration was 20 min, after which rats were placed in the arena of the experimental field.

The arena of the behavioral setup was represented by a round field 97 cm in diameter, divided into three annular areas: external, intermediate, and internal. The outer ring was additionally divided into 12 sectors, the intermediate one into 6 sectors, and the inner one stayed undivided, forming 19 equal sectors of 389 cm2 each. The illumination was set at 320 lx. After the rat was placed in the OF and the experimenter left the room, the behavior was recorded for 3 min on a VideoMot2 video system (TSE Systems; Germany) installed above the arena. Video recordings were made between 12:00 and 14:00, related to the periods of activity in rodents' circadian rhythms. The recording camera was controlled remotely.

Analyzed parameters included forward movement, turns, rearing with or without support, exploration of holes, and grooming.

After the completion of the entire set, 30 video records were obtained reflecting the behavior of rats in control, phenazepam and haloperidol groups. The records were processed using the OpenCV library in the Google Colaboratory service. Using a program code written in Python, each video was processed. The resulting video files included images consisting of two time positions expressed with color-coding. Green color corresponded to the present time and red - to the future (in 50 frames, i.e. 1.66 s). The time interval of 1.66 s was selected empirically in such a way, firstly, it is reliable to separate implemented action in the future from action in present, secondly, to keep connection with the current position because in more than 1.7 s, the location could be changed too much. The purpose of color coding was to create images that display 2 time positions of the rat at once: the present and the future. This approach made it possible to identify the following dynamic patterns in the future positions in relation to the present one: forward movement, turns of head or the entire body to the right and left, turn back.

In addition to the described method for identifying dynamic patterns, an extended analysis tool was used to trace the locomotor activity of animals at the different stages of recording. We were able to identify the following characteristics: movement in a circle or along a broken line, on the periphery or within the center of the arena, with or without periods of freezing. For this purpose, a Java code was created in the Fiji program from ImageJ software. Using the code, 540 sequential frames were obtained from video files and processed. Before extraction, these frames were converted to 32-bit using a median filter. The processing of 540 frames was carried out with a step of 10 frames (i.e., every 10th frame along the entire recording), using the physics color filter. All 540 frames were divided into 6 consecutive fragments, of 32 s, with 90 extracted frames in each fragment. Thus, six fragments reflected the behavioral activity of individual animals during the 3 min recording. Fragments mounted sequentially in a collage of 6 images made it possible to judge the change in the dynamics of the behavior of animals as they get used to the OF.

The data were statistically processed using one-way ANOVA analysis with post-hoc Tukey test, Student's t-test or Mann – Whitney U-test using SciPy library for python 3 (open source), PAST 4.03 and Excel 2016 (Microsoft, USA). Normality of data distribution in the samples was assessed using the Shapiro – Wilk test. Intergroup differences were considered statistically significant at $p < 0.05$. Data in bar charts are presented as $M \pm SEM$.

3 Result

The diverse effects of haloperidol and phenazepam can obscure the effect on anxiety of these drugs, leading to varying expressions of their effects. Identifying specific behavioral traits requires creating a structured behavioral profile. This profile can be composed by examining:

1. Spatial Movements: Observing animal movement in N-dimensional space by mapping intersections within certain areas, tracking time spent in these areas, assessing movement trajectories, measuring acceleration and deceleration, and analyzing movement frequency and direction.
2. Body Movements: Evaluating individual and combined body movements such as tail and head movements, and analyzing gaits.
3. Complex Behavioral Reactions: Studying behaviors like standing on hind legs with or without support, sniffing burrows, walls, floors, and air, and grooming behaviors.
4. Autonomic Responses: Monitoring urination and defecation patterns.

To construct a behavioral profile under drug influence, we initially focused on complex behavioral patterns, crucial for anxiety assessment. We expected distinct alterations in self-grooming, a well-known anxiety-related behavior, yet no quantitative differences in grooming were observed between groups. Notably, reduced complex behavioral patterns were observed in both drug groups compared to the control, particularly diminished hole sniffing and air sniffing in the phenazepam group, and reduced rearing (standing on hind legs) exclusively in the haloperidol group.

The limited changes in these behavioral patterns may be attributed to several factors. Firstly, the drugs may lack effects on anxiety. Secondly, they might influence the motor expression of anxiety-related behaviors rather than anxiety levels directly. Lastly, the recording duration (3 min) was shorter than standard open field test durations (5–10 min), mainly due to decreased activity in drug-administered groups. By the 4th minute, rats in the drug groups exhibited markedly reduced behavioral variety and became largely immobile. Such shortened recording periods make it challenging to derive statistically significant results solely from infrequent complex behaviors.

Further investigation of rat behavior required identifying patterns that could be quantitatively measured to draw statistically reliable conclusions. These behavior patterns might include simpler activities related to the rat's overall activity, its movements, or movements of specific body parts. In the classic approach of assessing anxiety-related behaviors using the open field test (OFT), a common method is to measure differences in the time spent and the number of crossings between the center and periphery sectors of the field.

Crossing into the center or periphery can be seen as exploratory behavior by the rat, influenced by its anxiety levels. Typically, higher anxiety levels (under normal central nervous system conditions) reduce the likelihood of crossing into the central sector. However, it's important to note that the number of crossings doesn't directly correlate with the time spent in these sectors. The time spent in a specific sector also follows a similar rule: the more anxiety expressed, the shorter the time spent in that sector. In our study, the total time rats spent in the center under the influence of haloperidol was significantly less compared to the control group (ANOVA $p < 0.05$, Post Hoc Tukey comparison $p < 0.05$). In the first minute, there was no difference between haloperidol, phenazepam, and control groups. However, by the second minute, both the phenazepam and haloperidol groups showed a substantial decrease in time spent in the center (and consequently, an increase in time spent in the periphery) (Fig. 1).

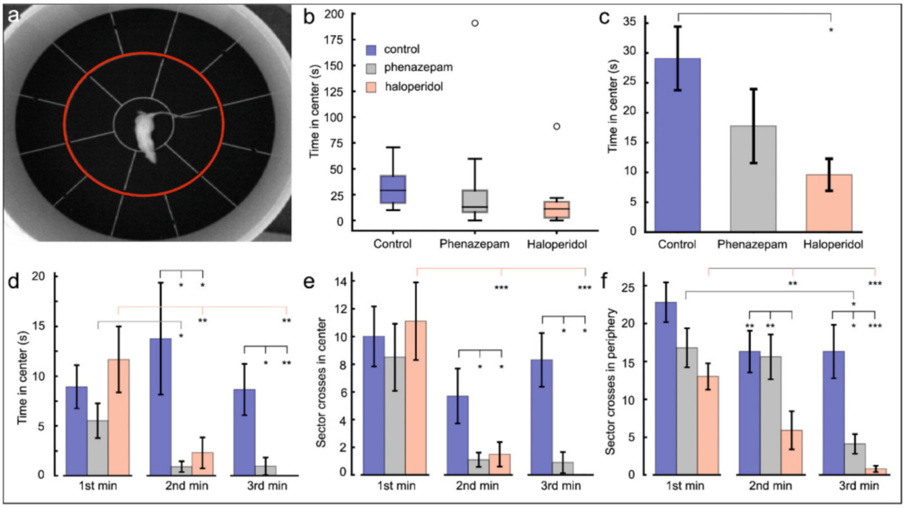

Fig. 1. Time, spent in the center. (a) Rat in the central sectors, red circle is a border for central sectors. (b) Boxplot with distribution of time spent in the central sectors during all the period of recording: outliers are included and shown as circles. (c) Comparison of all period of time spent in the center (One-way ANOVA, $F = 3.9$, $p = 0.034$). (d) Dynamic of time spent in the central sectors. 2nd minute: one-way ANOVA $F = 3.9$, $p = 0.02$ (post-hoc Tukey: control > phenazepam $p = 0.037$, control > haloperidol $p = 0.038$). 3rd minute: one-way ANOVA $F = 7.6$, $p = 0.002$ (post-hoc Tukey: control > phenazepam $p = 0.18$, control > haloperidol $p = 0.032$). Ingroup comparison of phenazepam 1st > 2nd, one-way ANOVA, $F = 3.9$, $p = 0.034$, ingroup comparison of haloperidol, one-way ANOVA, $F = 8.13$, $p = 0.002$ (post-hoc Tukey: 1st > 2nd – $p = 0.0086$ and 1st > 3rd – $p = 0.0033$). (e) Dynamic of sector crosses in center. 2nd minute: one-way ANOVA $F = 7.5$, $p = 0.002$ (post-hoc Tukey: control > phenazepam $p = 0.007$, control > haloperidol $p = 0.0056$). 3rd minute: one-way ANOVA $F = 11.3$, $p = 0.0003$ (post-hoc Tukey: control > phenazepam $p = 0.0021$, control > haloperidol $p = 0.0004$). Ingroup comparison of haloperidol, one-way ANOVA, $F = 12.9$, $p = 0.0001$ (post-hoc Tukey: 1st > 2nd – $p = 0.0009$ and 1st > 3rd – $p = 0.0002$). (f) Dynamic of sector crosses in periphery. 2nd minute: one-way ANOVA $F = 7.5$, $p = 0.002$ (post-hoc Tukey: control > phenazepam $p = 0.007$, control > haloperidol $p = 0.0056$). 3rd minute: one-way ANOVA $F = 11.3$, $p = 0.0003$ (post-hoc Tukey: control > phenazepam $p = 0.0021$, control > haloperidol $p = 0.0004$). Ingroup comparison of phenazepam 1st > 2nd, one-way ANOVA, $F = 4.0$, $p = 0.03$ (post-hoc Tukey: 1st > 3rd – $p = 0.044$, U-Manna: 1st > 2nd = 0.27), ingroup comparison of haloperidol, one-way ANOVA, $F = 12.7$, $p = 0.0001$ (post-hoc Tukey: 1st > 2nd – $p = 0.0023$ and 1st > 3rd – $p = 0.0002$). (* - $p < 0.5$, ** - $p < 0.01$, *** - $p < 0.001$).

The pattern of sector crossings showed a similar trend for the central sectors across the groups. However, when analyzing intersections in the peripheral sectors, a notable difference emerged between the haloperidol and phenazepam groups. In the haloperidol

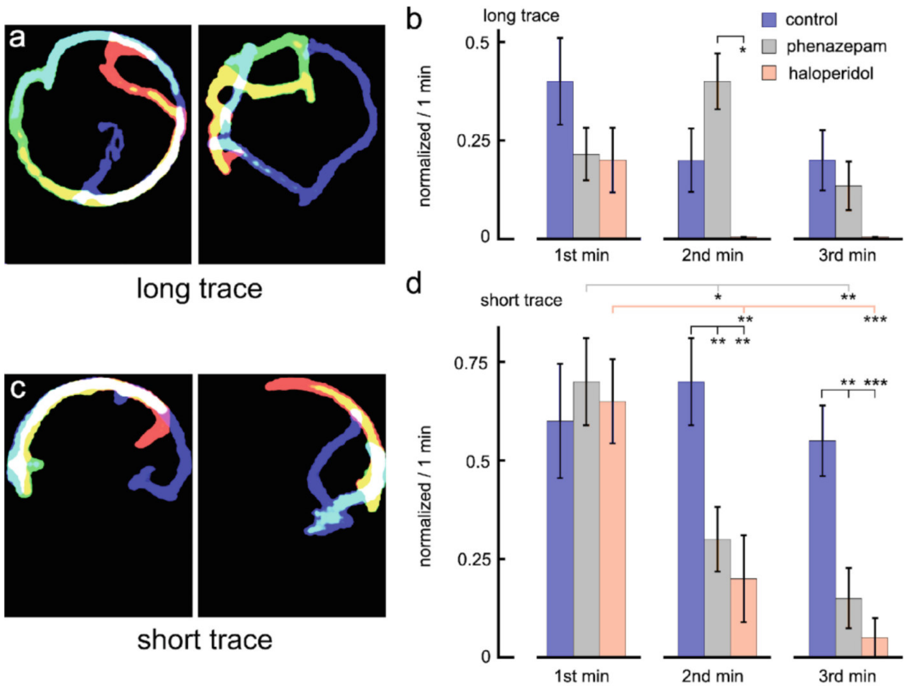

Fig. 2. Color-tracing analysis allows to distinguish between long (a) and short (c) runs, limited mobility within a small area (spot, e) and freezing (g) as specific patterns. (b) The dynamics of long runs are notable only for the predominance of phenazepam compared to haloperidol at the 2nd minute (One-way ANOVA: $p = 0.03$, post-hoc Tukey: $p = 0.025$). (d) A decrease in short runs after 1st minute was detected in the phenazepam (One-way ANOVA: $p = 0.0018$, post-hoc Tukey: $p = 0.024$ and $p = 0.0017$ for 2nd and 3rd minutes respectively) and haloperidol groups (One-way ANOVA: $p = 0.0003$, post-hoc Tukey: $p = 0.0056$ and $p = 0.0003$ for 2nd and 3rd minutes respectively). In the control group, the number of short runs did not change over time but was significantly higher in relation to phenazepam and haloperidol at the 2nd and 3rd minutes. (f) Spot activity in control group looked increasing but not statistically proven, while haloperidol showed a significant increase at the 2nd minute (One-way ANOVA: $p = 0.0038$, post-hoc Tukey: $p = 0.0026$), also differing from control and phenazepam at this particular time period (One-way ANOVA: $p = 0.00025$, post-hoc Tukey: $p = 0.0003$ and $p = 0.0029$ for control and phenazepam respectively). (h) Freezing was not typical for the control group at any time interval, but increased significantly from 1st by the 3rd minute in phenazepam (One-way ANOVA: $p = 0.02$, post-hoc Tukey: $p = 0.016$) and haloperidol (One-way ANOVA: $p = 0.00015$, post-hoc Tukey: $p = 0.0001$ and $p = 0.0044$) group. Haloperidol showed a slightly steeper increase in freezing than phenazepam, so a significant difference was observed between the 2nd and 3rd minutes ($p = 0.0044$). (* - $p < 0.5$, ** - $p < 0.01$, *** - $p < 0.001$).

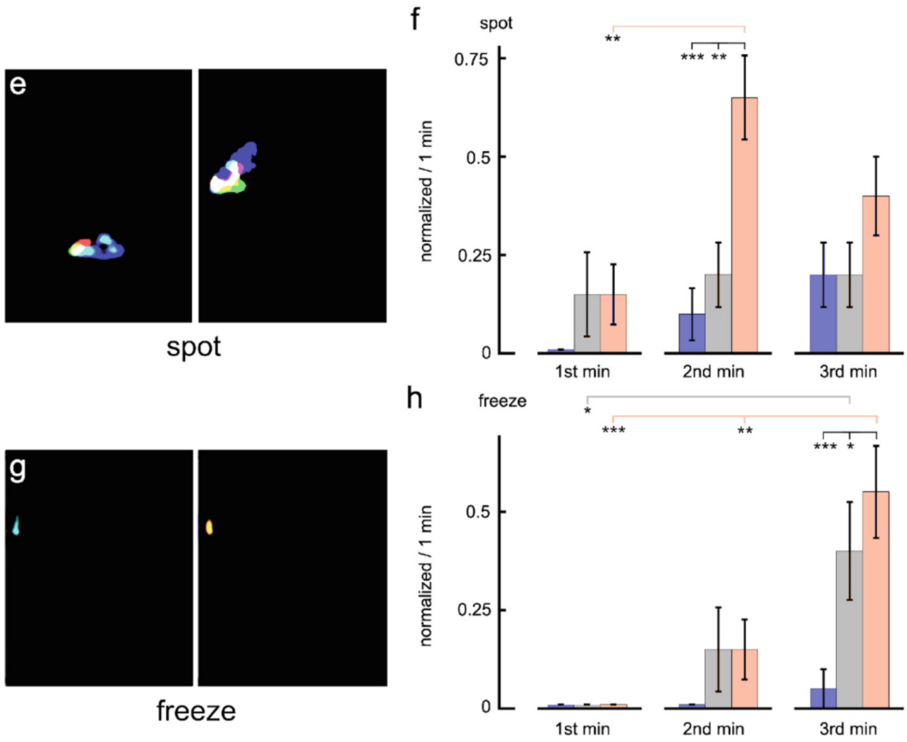

Fig. 2. (*continued*)

group, there was a statistically significant decrease in peripheral sector intersections starting from the 2nd minute (similar to the central sectors). Conversely, in the phenazepam group, a mild decrease in peripheral sector intersections was observed, beginning from the 3rd minute.

In addition to traditional methods, we employed a color-tracing technique to gain further insights into activity patterns, generating sequential images with colored traces of rat movement. By dividing the video into six equal parts (30-s intervals each), we obtained images with detailed information about the trajectory and movement patterns. To facilitate analysis, we categorized these images into four types based on the distance traveled: long path (> 3/4 of the trajectory), short path (< 3/4 of the trajectory), spot activity, and freezing. Our analysis revealed distinctive temporal changes in these patterns among the pharmacological groups, unlike the control group. Both the haloperidol and phenazepam groups exhibited a shift from movement along long or short paths to spot activity or freezing. Notably, phenazepam activity was characterized by sustained long routes, a statistical difference observed primarily compared to haloperidol at the 2nd minute of recording. These extended routes under phenazepam showed simple trajectories (is not shown) and tended to localize along the walls, aligning with previous observations on the stereotypical motor activity induced by phenazepam [44]. Conversely, haloperidol demonstrated a sudden increase in spot activity by the 2nd minute of recording (Fig. 2).

The data presented so far highlight notable changes in animal activity under the influence of drugs. The observed differences in peripheral activity suggest distinct mechanisms affecting overall behavior.

Using color coding, we identified initiation patterns of actions by processing video frames and overlaying the rat's position at a complete stop with its position 1.6 s later, indicating one of four actions: moving forward, turning back (180 degrees), turning to the side (approximately 90 degrees), or turning its head. These motor patterns occur frequently enough to allow for reliable analysis. However, assessing these patterns in the central sectors was only feasible during the first minute of recording when the pharmacologically treated rats were still quite active. Simply counting these patterns lacks specificity for a differentiated study between the center and periphery due to factors that may influence time spent in the center but are unrelated to anxiety. Therefore, we normalized these patterns to obtain their frequency in the center versus periphery. Additionally, we considered the relative prevalence of each pattern within groups. These selected motor patterns notably dominated over other behaviors such as grooming, sniffing, or standing on hind legs, suggesting that when a rat stops, its subsequent movement typically

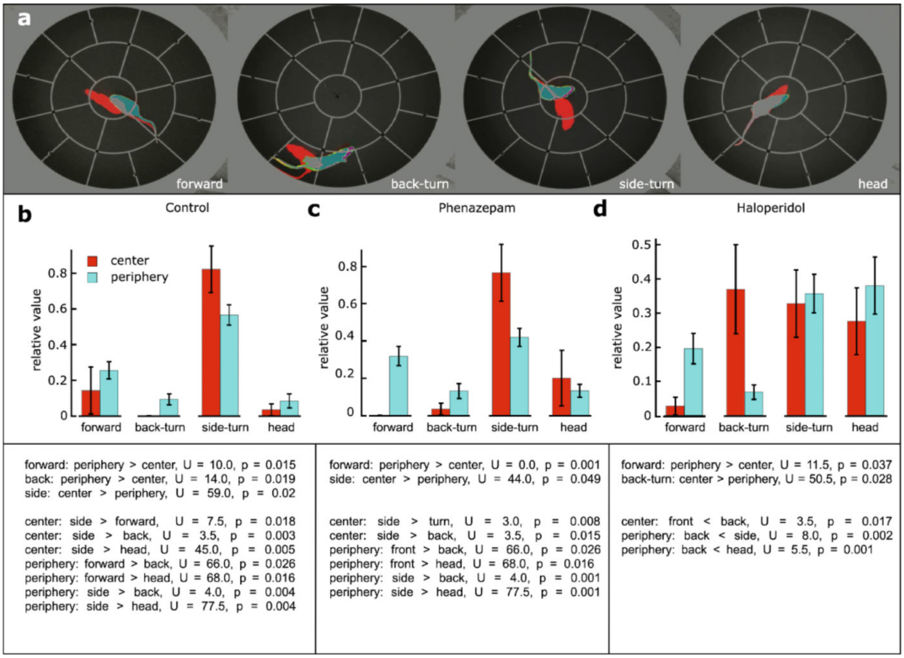

Fig. 3. Color-coding analysis of movement initiation patterns. (a) Examples of all initiation pattern. Initiation pattern of (b) control, (c) phenazepam and (d) haloperidol groups in center (red) and periphery (bright-green). All patterns values are relative part to the summary number of initiations. U Mann-Whitney test was used for statistical measurements.

follows one of these four scenarios. This analysis provides insight into the predominant type of movement initiation, directly reflecting the state of the central nervous system and anxiety levels.

Comparing these indicators for each pattern within groups reveals distinct behavioral profiles. The control and phenazepam groups show a preference for turns over other movement types in the center of the open field. In the periphery, forward movements are more frequent across all groups, indicating similar behavior between control and phenazepam groups except for a reduced proportion of turning movements due to increased forward movement. The behavioral structure of the haloperidol group differs significantly from the others, both in the center and periphery. In the center, there is no clear dominant pattern of behavior: back-turns, side-turns, and head-turns occur equally and slightly more frequently than forward movements. Back-turns are notably more prevalent in the center compared to other groups. On the periphery, all patterns except back-turns are distributed almost equally. Back-turns are significantly less frequent on the periphery and do not differ from other groups in this area (Fig. 3).

4 Discussion

The study elucidated the effects of phenazepam and haloperidol in the open field test. Our primary objective was to study their comparative influences on anxiety. Conventionally, behavioral assessments in the open field test span a minimum duration of 5 min, with particular emphasis on the initial moments for anxiety exploration and the evaluation of anxiolytic drug responses [45, 46]. The conventional methodology involves the evaluation of intricate behavioral patterns such as grooming, sniffing, stretching, and rearing, alongside the analysis of motor activity in terms of time spent and intersections within different zones. In our investigation, we supplemented these techniques with color-tracing and color-coding methodologies. Our findings unveiled a consistent trend in behavioral alterations within the phenazepam and haloperidol groups as compared to the control group. Both drug-treated cohorts exhibited a reduction in locomotor activity, albeit accompanied by nuanced discrepancies in other parameters. We observed that phenazepam's suppressive effect on activity manifested later and was counteracted by prolonged traverses along the periphery. Conversely, the activity decline in the haloperidol group was evident by the 2nd minute, partially compensated by localized movements and head rotations. Furthermore, our analysis delineated distinctive patterns in movement initiation between the phenazepam and haloperidol groups compared to the control. Rats administered with phenazepam displayed a slight deviation from the control in movement initiation, with a propensity towards forward movement in the peripheral areas. In contrast, the haloperidol group exhibited no dominant initiation type both in the center and periphery.

The decrease in locomotor activity observed in the open field test may indeed suggest heightened anxiety. Typically, behaviors such as freezing and thigmotaxis are associated with anxiety in this paradigm, particularly during the first minutes of the test. In our study, both the phenazepam and haloperidol groups exhibited reduced exploration of central sectors by the 3rd minute, coupled with an increase in freezing behavior, as indicated by color tracing. This raises the question: do phenazepam and haloperidol exacerbate rather than alleviate anxiety? On one hand, the introduction of psychotropic drugs induces a novel and unpredictable state in the nervous system, potentially eliciting or amplifying anxiety in rats confronted with a new and unfamiliar environment. On the other hand, the observed decrease in overall activity following phenazepam administration is attributed to the activation of widespread benzodiazepine receptors, leading to inhibition across various brain regions including the reticular formation and cortex [18]. Haloperidol, on the other hand, primarily impacts the dopaminergic system, antagonizing receptors in the nucleus accumbens and dampening motivation for engagement in diverse activities [47]. Notably, the decline in movement across the field in the haloperidol group was offset by an increase in localized activity and head turns, indicating the preservation of exploratory behavior. However, blockade of dopaminergic receptors in the striatum may result in rigidity, posing an additional barrier to normal task performance [47, 48]. Hence, while reduced locomotor activity in response to our selected pharmacological interventions may coincide with alterations in anxiety, it cannot be reliably regarded as a definitive indicator of such changes. The reduction in visits to central sectors could be indicative of increased anxiety, but it's essential to consider the broader context. In the haloperidol group, where both central and peripheral movements decreased, this decline seems more linked to a general reduction in activity rather than solely heightened anxiety. In contrast, rats in the phenazepam group displayed a distinct behavioral pattern. By the second minute, while peripheral movement persisted, activity in the central sectors notably decreased in both duration and frequency compared to the control group. This divergence suggests a potential increase in anxiety, yet such an interpretation overlooks the impact of phenazepam on the structural features of the brain. Our previous findings have highlighted that prolonged near-wall runs, a behavior observed under phenazepam influence, are associated with stereotypical behavior in rats [44]. This inference was drawn from the consistency of near-wall runs and the alignment of tail and head movements. The predictability of behavior in the phenazepam group, thus, may stem from the inhibition of cortical processes responsible for movement planning [49, 50]. Therefore, while the reduction in visits to central sectors under phenazepam influence may imply heightened anxiety, it also reflects the drug's influence on neural mechanisms governing behavior.

Changes in the composition of initiated actions can indeed provide insights into alterations in anxiety levels, although they are influenced by multiple factors beyond anxiety alone. Firstly, the positioning relative to the cage wall plays a crucial role. Across all three groups, initiating movements towards the movement along the longitudinal axis of rat (i.e., forward) is more prevalent in the periphery than in the center. This tendency stems from the lower probability of turning towards the wall compared to choosing to turn towards the open arena or continuing along the periphery. Secondly, the characteristics of drug influence significantly impact initiated movements. In the haloperidol group, the absence of distinct patterns and a wide dispersion of values in the ratio of initiated actions is evident. This variability is attributed to reduced movement activity and a compensatory increase in lateral head turns. Particularly noteworthy are the turns initiated in the center, a behavior observed primarily during the initial minute of recording. This behavior may reflect heightened anxiety and the need to protect one's rear in a novel environment, suggesting a potential link between anxiety and specific movement patterns. In summary, while changes in the composition of initiated actions can provide valuable insights into anxiety-related alterations, their interpretation requires consideration of various factors including environmental context, drug effects, and individual behavioral tendencies.

5 Conclusions

The findings from our analysis of rat behavior under the influence of phenazepam and haloperidol in a 3-min open field test highlight a notable disparity between the animal's anxiety state and its motor activity level. This disconnection between emotional arousal and overall activity bears significant implications for clinical practice, suggesting that a reduction in psychoemotional arousal and general activity following administration of antipsychotics and tranquilizers does not invariably signify the drugs' anxiolytic efficacy. Preserving the emotional component of anxiety while suppressing overall activity may have adverse consequences on a patient's mental well-being and recovery trajectory. It underscores the importance of not solely relying on motor activity as a measure of anxiety alleviation but also considering the emotional dimension of anxiety in clinical assessments and treatment evaluations. This nuanced understanding is crucial for optimizing therapeutic strategies and ensuring comprehensive care for patients undergoing psychiatric treatment.

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