

Memory and Learning in WAG/Rij and Sprague Dawley Rats: Investigating the Effect of “Racial Experience,” Especially on Predisposition to Epilepsy

WAG/Rij ve Sprague Dawley Sıçanlarında Hafıza ve Öğrenme: “İrksal Deneyimin” Özellikle Epilepsi Yatkınlığının Üzerindeki Etkisinin Araştırılması

Burcu ÇEVRELİ¹
Öznur Özge ÖZCAN²



¹Department of Physiology, Faculty of Medicine, Neuropsychopharmacology Practice and Research Center, Üsküdar University, Istanbul, Türkiye

²Department of Molecular Biology and Genetics, Faculty of Engineering and Natural Sciences, Üsküdar University, Istanbul, Türkiye



Geliş Tarihi/Received :17.03.2025
Kabul Tarihi/Accepted :03.09.2025
Yayın Tarihi/Publication Date :19.09.2025

Sorumlu Yazar/Corresponding author:
Burcu Çevreli

E-mail: burcu.cevreli@uskudar.edu.tr

Cite this article: Çevreli, B., & Özcan, Ö.Ö. (2025). Memory and Learning in WAG/Rij and Sprague Dawley Rats: Investigating the Effect of “Racial Experience,” Especially on Predisposition to Epilepsy. *Journal of Laboratory Animal Science and Practices*, 5(2), 102-109.
<https://doi.org/10.62425/jlasp.1660043>



Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

ABSTRACT

This research sought to investigate how genetic variations influence learning, short-term memory, and long-term memory in rats. In particular, it compared *WAG/Rij* (WR) rats, which are naturally prone to epilepsy, with *Sprague-Dawley* (SD) rats. A total of 24 male rats, consisting of 12 SD and 12 WR rats, were evaluated using an eight-arm radial maze to examine spatial memory and the retention of learning over time. No significant differences were observed in working memory error (WME) at 48, 72, 96, 120, and 144 hours ($p > .05$), and similar results were found for reference memory error (RME). However, WR rats made significantly more RME than SD rats at 48 hours ($p = .0111$, 95% CI: -1.606 to -0.2178). SD rats also completed the maze significantly faster at 96 hours ($p = .0094$) and 120 hours ($p = .0383$) than WR rats. Additionally, on the 4th day of the acquisition trial, WR rats made significantly more total error than SD rats ($p = .0045$). This research offers fresh perspectives on the variations in learning and memory across different rat strains within various behavioral models. Although SD rats gave better results in short-term memory and faster results in the process of completing the task compared to WR rats, further research is recommended in different behavioral patterns.

Keywords: Racial experience, Reference memory, Spatial learning, Working memory.

Öz

Bu araştırmada genetik varyasyonların sıçanlarda öğrenmeyi, kısa süreli hafızayı ve uzun süreli hafızayı nasıl etkilediğinin araştırılması amaçlandı. Özellikle, doğal olarak epilepsiye yatkın olan *WAG/Rij* (WR) sıçanlarını *Sprague-Dawley* (SD) sıçanlarıyla karşılaştırmıştır. 12 SD ve 12 WR sıçanından oluşan toplam 24 erkek sıçan, uzaysal hafızayı ve zaman içinde öğrenmenin tutulmasını incelemek için sekiz kollu bir radyal labirent kullanılarak değerlendirilmiştir. 48, 72, 96, 120 ve 144. saatlerde çalışma belleği hatalarında (WME) anlamlı bir fark gözlenmemiştir ($p > .05$) ve referans bellek hataları (RME) için benzer sonuçlar bulunmuştur. Bununla birlikte, WR sıçanları 48. saatte SD sıçanlarına göre anlamlı derecede daha fazla RME yapmıştır ($p = .0111$, %95 GA: -1,606 ila -0,2178). SD sıçanları ayrıca labirenti 96 saatte ($p = .0094$) ve 120 saatte ($p = .0383$) WR sıçanlarından önemli ölçüde daha hızlı tamamladı. Ek olarak, edinim denemesinin 4. gününde, WR sıçanları SD sıçanlarından önemli ölçüde daha fazla toplam hata yaptı ($p = .0045$). Bu araştırma, çeşitli davranış modelleri içindeki farklı sıçan türleri arasında öğrenme ve bellekteki farklılıklar hakkında yeni bakış açıları sunmaktadır. SD sıçanları kısa süreli bellekte daha iyi sonuçlar ve görevi tamamlama sürecinde WR sıçanlarına kıyasla daha hızlı sonuçlar vermiş olsada, farklı davranış kalıplarında daha fazla araştırma yapılması önerilmektedir.

Anahtar kelimeler: Çalışma belleği, İrksal deneyim, Mekansal öğrenme, Referans belleği.

Introduction

Rats are the most commonly used animal group in scientific research, particularly in biotechnology and health-related studies. Rats, which vary in size and tail length, are widely used in various fields, including basic medicine, pharmacology, food science, and behavioral research (Gou et al. 2024). Many of the inbred rat strains used today can be traced back to the *Wistar Albino* lineage. Among these, the *Sprague Dawley* (SD) rat is the most frequently employed species in pharmaceutical research, particularly in the United States and Japan (Caine et al. 2023). In comparison to laboratory mice, fewer rat species are commonly used in biomedical studies. Another widely utilized strain is the well-established *Wistar Albino* rat. Additionally, the *Wistar Albino Glaxo* from *Rijswijk* (WAG/Rij) rat, originally developed as an epilepsy model, has since been employed in the study of various related conditions. This inbred strain, known as WAG/Rij (WR), is specifically associated with genetic absence epilepsy, a non-convulsive form of the disorder (Sitnikova, 2024). Various breeds of laboratory animals are commonly used in behavioral studies; however, it is essential to consider that inherent traits may vary due to genetic differences between strains (Bárdos et al., 2024).

Behavior is closely linked to brain function, and variations in cognitive abilities among different strains can affect experimental outcomes, potentially leading to inconsistencies across research groups (Sarmiento et al. 2024). Therefore, it is essential to conduct behavioral phenotyping on laboratory animals from various strains to ensure that results are reliable and comparable (Kovarova et al. 2025). In studies of learning and behavior, related and wild-type strains of albino rats are commonly produced and utilized in neurobiological and physiological research, particularly concerning the nervous system and learning processes. This research often translates to understanding mechanisms underlying human behavior, especially memory and learning. Given that rats and mice are similar in their natural behavior and typically inhabit underground burrows resembling complex mazes, they are particularly favored in studies focused on spatial learning and memory. Researchers often assess these learning behaviors using various maze types, such as the radial arm maze, which can be adapted through different behavioral tasks and arm configurations (Peleh et al. 2019; Wijnen et al. 2024).

Spatial working memory refers to the temporary retention of a limited amount of spatial information, allowing for immediate access and use in various cognitive processes. Spatial reference memory refers to spatial information that is consistently utilized and typically acquired through

repeated training. Over time, this information becomes consolidated, making it more resistant to interference (McQuail et al. 2021). The interplay of environmental influences, genetic factors and biochemical variations in neural connections contributes to the observed differences in learning and memory capabilities among individuals and across species in both humans and animals (Gökçek-Saraç et al. 2012; Lee & Jung 2014).

Behavioral differences have been widely studied in experimental animals. Research indicates notable variations in cognitive task performance among different breeds. For instance, Jaramillo and Zador reported that comparing *Long Evans* (LE) rats and *C57Bl/6J* mice on the flexible sound-categorization task, the rat species learned the task faster than mice (Jaramillo & Zador, 2014). In another study, Blankenship et al. compared morris water task performance in rats and prairie voles. Rats demonstrated superior performance compared to prairie voles in critical aspects of the task, such as the time taken to locate the platform, the efficiency of their swim paths, and the level of directional accuracy. These differences could stem from variations in spatial cognition, stress response, physiology, or motivation among the species (Blankenship et al. 2019). The radial arm maze (RAM) has been widely utilized to investigate spatial cognition, memory, and learning in rodents (Kohler et al. 2022). Research comparing potential breed-related differences in rats, especially using the radial arm maze (RAM), is relatively limited. The RAM is beneficial for simultaneously evaluating working or reference memory. For example, Gökçek-Saraç et al. conducted a study that examined the performance of various rat breeds in the RAM. Their findings indicated that *Wistar/Sprague-Dawley* (W/SD) rats made fewer reference memory error and acquired tasks more quickly than both outbred LE and Wistar rats. Moreover, Wistar rats exhibited fewer mistakes in working memory tasks than other strains (Gökçek-Saraç et al. 2015). The WR rats are an inbred genetic epilepsy model for animal studies showing absence-like epilepsy. The established impact of epilepsy on learning and memory (De Deurwaerdère et al. 2022; Casillas-Espinosa et al. 2024), along with the limited cognitive assessments of animal models for absence epilepsy, inspired our study. We assessed the learning and memory capabilities of WR rats against age-matched Sprague-Dawley control rats using a thoroughly validated RAM. To date, no studies have directly compared spatial and working memory between WR rats and SD rats.

This study aimed to examine variations in working and reference spatial memory at both the individual and breed levels between two widely used laboratory rat strains such as WR and SD rats, by utilizing various performance metrics in the RAM.

Methods

This study involved a total of 24 male rats divided 12 male SD and 12 male WR rats, each 15 months old and weighing between 350-400 grams, with a maximum age difference of 10 days between individuals. All procedures adhered to the guidelines established by the U.S. National Institutes of Health as outlined in the Guide for the Care and Use of Laboratory Animals (OECD 423). Two male rats were housed in standard cages using sawdust under a 12-h light/dark cycle. Water and ad libitum were provided. Their diet consisted of pellet food formulated to meet their physiological needs. Prior to the initiation of the experimental procedures, an official application was submitted to the Üsküdar University Animal Experiments Ethics Committee, and approval was obtained (Approval Date: 21.12.2023, Approval Number: 2023-09).

Eight-Arm Radial Maze

This approach is commonly employed in behavioral studies to assess spatial memory. It features eight horizontal arms, each measuring 57x11 cm, that extend evenly from a central platform elevated 80 cm off the ground. Each arm is equipped with an automatic door that stands 20 cm tall at its entrance. The entire structure, including the platform and doors, is constructed from opaque gray Plexiglas. The maze features eight distinct visual cues, with four near the central platform and four on the walls of the arms. These cues vary in shape (square, rectangle, circle, and triangle) and color (yellow, green, purple, and red). The setup is illuminated from above, ensuring visibility. At the end of each arm, food rewards consisting of beet sugar-coated cornflakes are placed. The test comprises three main stages: (1) a three-day habituation phase, where subjects undergo a 15-minute exploration period to become familiar with the maze, (2) an acquisition phase lasting eight days, during which two consecutive five-minute trials are conducted daily, and (3) an experimental phase that includes a single five-minute trial performed at intervals of 48, 72, 96, 120, and 144 hours following the last session. During all phases except for the initial exploration, food rewards are placed in only four of the arms. At the beginning of each trial, the rats are briefly restrained for 30 seconds before being placed on the central platform, where they can move freely until all the food is retrieved. The trial lasts for five minutes. A rat's visit to an arm is recorded when all four paws enter it. If the rat goes into an arm that was previously inaccessible, it is classified as a reference memory error (RME).

Conversely, if the rat re-enters an arm that it has already visited, this is considered a working memory error (WME). Performance is assessed by measuring the time taken to locate the four accessible arms and by tallying the total occurrences of working, reference, and overall memory error during the trials (Kohler et al. 2014).

Statistical Analysis

Data analysis was conducted using GraphPad Prism 10.0 (GraphPad Software, San Diego, CA). Normality of the distribution was conducted by descriptive analysis. To examine time-dependent differences between groups, mixed-effects ANOVA was used followed by LSD post hoc test. Statistical significance was defined as $p < .05$. The results are presented as mean \pm SEM.

Results

Performance Data Across Groups

The study examined performance indicators including total error and total completion time. Additionally, WME and RME were evaluated between WR and SD rat strains and the different time frames were compared. All results given in Table 1.

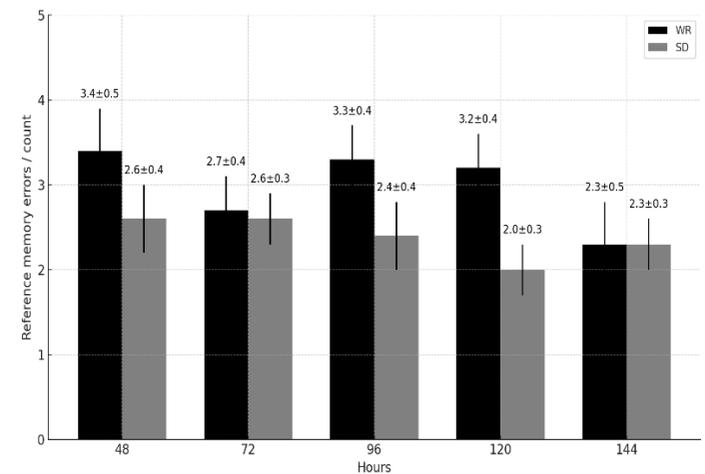


Figure 1. The results of eight arm radial maze which illustrate the reference memory error. Data are presented as mean \pm S.E.M., and a mixed-effects ANOVA was conducted, followed by post hoc LSD tests. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

Şekil 1. Referans bellek hatalarını gösteren sekiz kollu radyal labirentin sonuçları. Veriler ortalama \pm S.E.M. olarak sunulmuştur ve karışık-desen ANOVA kullanılmış, ardından post hoc LSD testleri yapılmıştır.

Table 1. Comparison of reference memory error, working memory error, session duration and total errors/count results on different acquisition trial days measured between SD and WR breeds in the eight-arm radial maze. A mixed-effects ANOVA * $p < .05$. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

Tablo 1. Sekiz kollu radyal labirentte SD ile WR ırkları arasında ölçülen farklı edinim deneme günlerindeki referans bellek hatası, çalışma belleği hatası, oturum süresi ve toplam hata/sayım sonuçlarının karşılaştırılması. Karışık-desen ANOVA. * $p < .05$.

Reference memory errors/count	Predicted (LS) mean difference	95% CI of difference	p value
48 h	-0.7879	-1.968 to 0.3927	.1862
72 h	-0.1212	-1.302 to 1.059	.8375
96 h	-0.9773	-2.158 to 0.2033	.1026
120 h	-1.167	-2.347 to 0.01392	.0527
144 h	0.01515	-1.165 to 1.196	.9795
Working memory errors/Count			
48 h	-0.9118	-1.606 to -0.2178	.0111*
72 h	-0.06219	-0.7562 to 0.6318	.8579
96 h	0.2031	-0.4909 to 0.8971	.5593
120 h	-0.2944	-0.9884 to 0.3996	.3982
144 h	0.3924	-0.3016 to 1.086	.2615
Session duration			
48 h	-5.485	-40.18 to 29.21	.7522
72 h	-12.52	-47.22 to 22.17	.4719
96 h	-46.65	-81.35 to -11.96	.0094*
120 h	-36.77	-71.46 to -2.069	.0383*
144 h	-26.17	-60.86 to 8.529	.1361
Total errors/count			
1 Day	-0.9167	-2.790 to 0.9565	.3329
2 Day	-1.25	-3.123 to 0.6231	.1878
3 Day	-0.6667	-2.540 to 1.206	.4806
4 Day	-2.75	-4.623 to -0.8769	.0045*
5 Day	-0.5833	-2.456 to 1.290	.537
6 Day	0.25	-1.623 to 2.123	.7911
7 Day	-0.3333	-2.206 to 1.540	.724

A mixed-effects ANOVA * $p < .05$. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

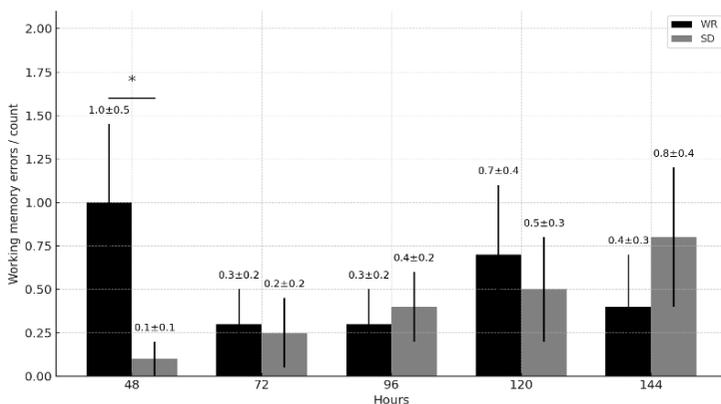


Figure 2. The results of eight arm radial maze which working memory error. Data are presented as mean \pm S.E.M., and a mixed-effects ANOVA was conducted, followed by post hoc LSD tests. * $p < .05$. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

Şekil 2. Çalışma belleği hataları olan sekiz kollu radyal labirentin sonuçları. Veriler ortalama \pm S.E.M. olarak sunulmuştur ve karışık-desen ANOVA kullanılmış, ardından post hoc LSD testleri yapılmıştır. * $p < .05$.

Results of mixed-effects ANOVA showed the RME during the learning stage, with training day as a within-subjects factor and experimental group. There was no significant main effects for training hours [$F(4, 44) = 1.033, p = .4010$], group differences [$F(1, 11) = 3.840, p = .0759$], or the interaction between group and training hours [$F(4, 39) = 0.8872, p = .4806$] (Figure 1). These findings suggest that RME rates remained consistent throughout the training hours and did not differ significantly between the groups.

Results of mixed-effects ANOVA showed the WME during the learning phase, maintaining training day as a within-subjects factor and experimental group. There was no significant main effects for training hours [$F(4, 44) = 0.5565, p = .6953$], group differences [$F(1, 11) = 0.7564, p = .4030$], or the interaction between training hours and group [$F(4, 39) = 2.151, p = .0927$] (Figure 2). This indicates that WME rates did not exhibit significant differences during the training intervals of 72, 96, 120, and 144 hours, and no notable disparities were found between the groups. However, at the 48-hour mark, the WR group had significantly higher WME rates compared to the SD group ($p = .0111, t = 2.639, 95\% \text{ CI: } -1.606 \text{ to } -0.2178$).

A mixed-effects ANOVA was performed to examine the total time taken (-on duration) during the training day, using training day as a within-subjects factor and experimental group as a between-subjects factor. The analysis did not reveal any significant main effects for hours [$F(4, 44) = 2.389, p = .0653$], session duration [$F(1, 11) = 3.159, p = .1032$], or the interaction between session duration and hours [$F(4, 39) = 2.480, p = .0597$] (Figure 3). These results suggest that the total time taken remained stable across training hours, with no significant differences between groups at 48, 72, and 144 hours. However, the SD group completed the 8-arm radial arm maze in a shorter duration compared to the WR group at 96 hours ($p = .0094, t = 2.701, 95\% \text{ CI: } -81.35 \text{ to } -11.96$) and at 120 hours ($p = .0383, t = 2.128, 95\% \text{ CI: } -71.46 \text{ to } -2.069$).

Additionally, another mixed-effects ANOVA indicated that the total error made during the completion of the 8-arm radial arm maze varied at different time points following the acquisition trial (Figure 4). A significant main effect was identified for acquisition days [$F(7, 77) = 12.24, p < .0001$] and for total error/count [$F(1, 11) = 6.917, p = .0234$]. However, no significant main effect was found for the interaction between acquisition trial and total error/count [$F(7, 77) = 0.9147, p = .4999$] (Figure 2). Importantly, the WR group made a significantly more total error than the SD group during the fourth acquisition trial day ($p = .0045, t = 2.923, 95\% \text{ CI: } -4.623 \text{ to } -0.8769$).

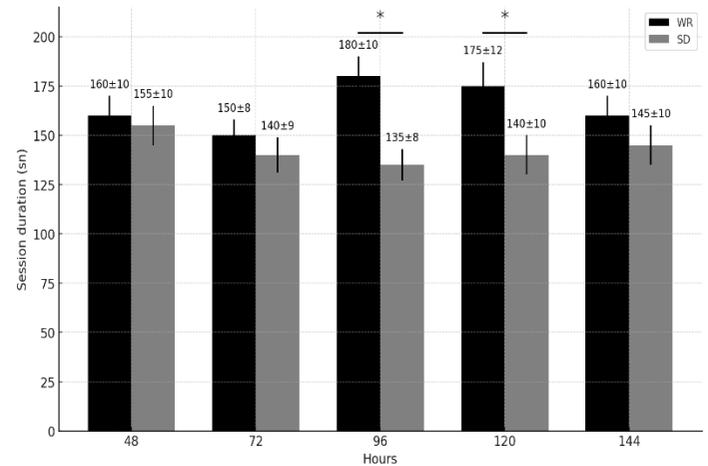


Figure 3. The total time for the session duration to complete the 8-arm radial arm maze. Data are presented as mean \pm S.E.M., and a mixed-effects ANOVA was conducted, followed by post hoc LSD tests. $*p < .05$. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

Şekil 3. 8 kollu radyal kol labirentini toplam tamamlama süresi. Veriler ortalama \pm S.E.M. olarak sunulmuştur ve karışık-desen ANOVA kullanılmıştır, ardından post hoc LSD testleri yapılmıştır. $*p < ,05$.

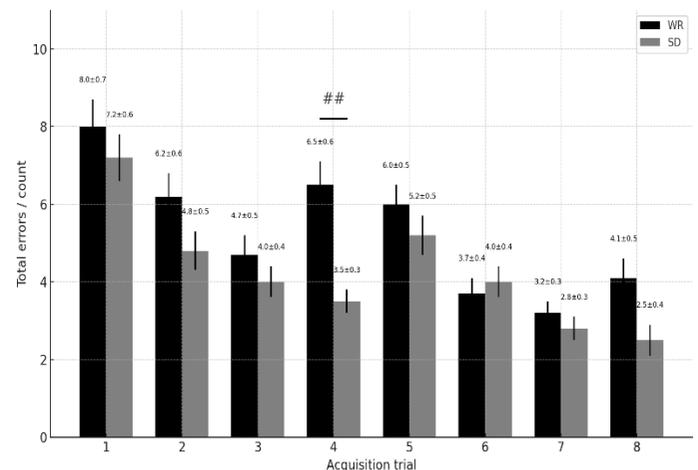


Figure 4. Total error count to complete the 8-arm radial arm maze was detected at different time points after the conclusion of the acquisition trial. Data are presented as mean \pm S.E.M., and a mixed-effects ANOVA was conducted, followed by post hoc LSD tests. $##p < .005$. SD: with *Sprague-Dawley* (SD) rats, WR: *WAG/Rij* rats.

Şekil 4. Toplam hata sayısı. Edinim denemesinin tamamlanmasından sonra farklı zaman noktalarında 8 kollu radyal kol labirentini tamamlamak için tespit edildi. Veriler ortalama \pm S.E.M. olarak sunuldu ve karışık-desen ANOVA kullanılmıştır, ardından post hoc LSD testleri yapıldı. $##p < ,005$.

Discussion

In this study, we examined WR rats, a widely recognized epileptic strain commonly utilized in behavioral research on learning and memory, alongside SD rats. Our results revealed notable strain-specific differences in performance on the RAM task. To assess working and reference memory separately, we compared the frequency of WME and RME between the groups. Furthermore, a mixed-effects ANOVA (group \times error \times hours) was conducted to analyze temporal variations in these error types concerning overall task completion and total error.

To our knowledge, we present the first study in the literature to report the results of learning and memory studies on rats of different breeds, especially those covering the old age period, comparing the inbred WR rat strain, known for its epilepsy tendency, with the SD rat strain. Another important point of the study was that the results were representative of the 15-month-old, translationally elderly, and provided important information for future studies on learning and memory in the elderly. This study investigated short and long-term spatial memory retention in rats using an eight-arm radial maze. When assessing spatial memory in SD and WR rats, no significant differences were observed in WME at 48, 72, 96, 120, and 144 hours and similar results were found for RME. However, at the 48-h, WR rats exhibited significantly more RME than SD rats. Additionally, SD rats completed the eight-arm radial maze significantly faster at 96 hours and 120 hours compared to WR rats. On the fourth day of the acquisition trial, WR rats had a significantly higher total error count than SD. These findings contribute to the understanding of learning and memory variations across different rat strains in various behavioral models. While SD rats demonstrated better short-term memory and completed tasks more quickly than WR rats, further research is necessary to explore these differences in other behavioral contexts. SD rats performed better than the WR type in the three criterion difference time periods (sessions, choices, and total error for criteria). WR rats had higher WME scores than SD rats, especially in the 48 hours. There were no significant differences between RME in the comparison, perhaps indicating that epilepsy susceptibility does not contribute much to the final behavioral outcome on working memory. Arm entry error can be divided into reference memory arms or working memory arms. When recategorized errors were examined, no significant difference was found in the reference memory arms. At this point, WR rats were consistently making more error than SD in the working error arms compared to WR rats at 48 hours. Interestingly, SD rats were making more error at

96 and 144 hours, but this difference was not significant. This pattern was also seen in the working memory arms, but did not produce significant differences across races. Thus, these results support the literature suggesting that WR has only a short-term selective deficit in working memory. These results bolster the idea that there is a notable difference between working memory and long-term memory, as suggested by current research examining spatially targeted genetic modifications in the forebrain and hippocampus. By evaluating the performance of different animals in spatial learning tasks, these studies allow for the independent measurement of working and RME (8,18,19). Variations in behavior among individuals and strains may arise from different factors. While environmental influences, such as upbringing and care conditions, can affect animal behavior, differences observed among well-established laboratory strains that adhere to standard animal care practices are more likely to have a genetic basis (Junttila et al. 2022). This is evident in WR rats, which showed distinctions in total time and total error while completing the arm maze task. Limited research has explored breed-specific differences in rats, especially utilizing the RAM, a tool that allows for the concurrent assessment of both working and reference memory. For example, Gökçek-Saraç et al. analyzed RAM performance across different rat breeds. Their findings indicated that *Wistar/Sprague-Dawley* (W/SD) rats made fewer RME and acquired tasks more quickly than both outbred LE and *Wistar* rats (Gökçek-Saraç et al. 2015). Furthermore, wistar rats showed a reduced incidence of WME when compared to other rat strains. Harker and Whishaw found that LE rats excelled over *Fisher-Norway* rats in spatial learning tasks conducted in a water maze. They also reported that *Fisher-Norway* rats had better visual acuity than LE rats (Harker & Whishaw, 2002). These results are consistent with other findings indicating that rat performance on well-established functional and mental memory tasks can be strongly influenced by environmental changes present in the experimental room (Ramos, 2000). In addition, in another study comparing the *Wistar* breed, which is frequently used in learning and memory studies, it was reported that *Hooded Lister* rats had significantly fewer WME and RME than *Wistar* rats, according to the results of the RAM experiment (Manahan-Vaughan & Schwegler, 2011). To our knowledge, in the preclinical literature, most of the existing studies focus specifically on pharmacological efficacy in racial differences (Bryda, 2013; Gao et al. 2021; Nollen et al. 2021; Russomanno et al. 2023), and relatively few studies have addressed differences in brain and behavior-focused cognitive functions but different memory methods at adult age of rats (Ellenbroek & Youn, 2016). In general evaluation, these previous studies

compared different behavioral platforms related to spatial, working, visual, location, reference memory in different rat strains covering the adult period (Vorhees and Williams, 2024). An important aspect that warrants further discussion is the neurophysiological basis through which the epileptic predisposition of WR rats might influence cognitive and behavioral performance. WAG/Rij rats are widely recognized as a validated model of absence epilepsy, primarily characterized by spike-and-wave discharges (SWDs) originating in the somatosensory cortex and thalamocortical circuits (Sitnikova, 2024). These spontaneous SWDs, even in the absence of overt motor seizures, have been shown to disrupt cortical information processing and interfere with attentional control and working memory (De Deurwaerdère et al., 2022). Studies using EEG recordings in WR rats have demonstrated that SWDs can transiently suppress neuronal firing in prefrontal and hippocampal regions, which are critical for spatial memory and executive function. This transient disruption may lead to increased cognitive errors during maze navigation tasks that require continuous updating of spatial information and flexible decision-making. Therefore, the higher working and total errors observed in WR rats, particularly during early retention intervals, may be attributed to impaired synchronization of hippocampal-prefrontal networks due to interictal epileptic activity. Furthermore, chronic epileptiform discharges have been associated with synaptic plasticity impairments and altered expression of NMDA receptor subunits in the hippocampus of WR rats, further compromising memory consolidation processes (Gökçek-Saraç et al., 2012). Taken together, these neurophysiological abnormalities likely contribute to the subtle but significant deficits in spatial learning and working memory observed in WR rats compared to their non-epileptic SD counterparts. The results indicate the need for further research on racial differences and at different stages of life, especially in maze experiments.

Conclusion

Overall, this study highlights spatial and functional learning differences between SD and WR rat strains, which are genetically related and associated with epilepsy susceptibility, and are widely used in studies of racial experience effects in learning and behavior. This study offers fresh insights into the variations in learning and memory among different rat strains across various behavioral models. While SD rats demonstrated superior short-term memory and completed tasks more quickly than WR rats, additional research is suggested to explore these differences in other behavioral patterns.

Ethics Committee Approval: Approval for all animal experiments was obtained from the Animal Research Ethics Committee of Üsküdar University, Istanbul, Turkey. The study received ethical approval from the Local Ethics Committee of Üsküdar University on December 21, 2023, under decision number Ü.Ü-HADYK 2023-09.

Author Contributions: Concept – BÇ, ÖÖÖ; Design - BÇ; Supervision - BÇ; Resources - BÇ; Materials - BÇ; Data Collection and/or Processing - BÇ; Analysis and/or Interpretation – BÇ; Literature Search - ÖÖÖ; Writing Manuscript – BÇ, ÖÖÖ; Critical Review – BÇ, ÖÖÖ.

Peer-review: Externally peer-reviewed.

Funding: No funding.

Declaration of Interests: The authors declare that no conflicts of any interest.

Acknowledgements: We acknowledge to the Experimental Research Neuropsychopharmacology Application and Research Center at Üsküdar University.

References

- Bárdos, B., Török, H. K., & Nagy, I. (2024). Comparison of the exploratory behaviour of wild and laboratory mouse species. *Behavioural Processes*, 217:105031. <https://doi.org/10.1016/j.beproc.2024.105031>
- Blankenship, P. A., Normann, M. C., Donaldson, T. N., Baumeister, J., McNeal, N., Grippo, A. J., & Wallace, D. G. (2019). Making waves: Comparing Morris water task performance in rats and prairie voles. *Behavioural Brain Research*, 360, 7–15. <https://doi.org/10.1016/j.bbr.2018.11.032>
- Bryda, E. C. (2013). The Mighty Mouse: The impact of rodents on advances in biomedical research. *Missouri Medicine*, 110(3), 207-211
- Caine, S. B., Plant, S., Furbish, K., Yerton, M., Smaragdi, E., Niclou, B., Lorusso, J. M., Chang, J. Y., Bitter, C., Basu, A., Miller, S., Huang, C. Y., Komson, R., Liu, D., Behar, S., & Thomsen, M. (2023). Sprague Dawley rats from different vendors vary in the modulation of prepulse inhibition of startle (PPI) by dopamine, acetylcholine, and glutamate drugs. *Psychopharmacology*, 240(9), 2005–2012. <https://doi.org/10.1007/s00213-023-06444-1>
- Casillas-Espinosa, P. M., Garcia-Olivares, J., Li, R., Li, C., Yu, C., Formella, A. E., & O'Brien, T. J. (2024). Huperzine A suppresses absence seizures in the genetic absence epilepsy rat from Strasbourg (GAERS) model of genetic generalized epilepsy with absence seizures. *Epilepsia Open*, 9(5):1826-1836. <https://doi.org/10.1002/epi4.13016>
- De Deurwaerdère, P., Casarrubea, M., Cassar, D., Radic, M., Puginier, E., Chagraoui, A., Crescimanno, G., Crunelli, V., & Di Giovanni, G. (2022). Cannabinoid 1/2 Receptor Activation Induces Strain-Dependent Behavioral and Neurochemical Changes in Genetic Absence Epilepsy Rats From Strasbourg and Non-epileptic Control Rats. *Frontiers in Cellular Neuroscience*, 16, 886033. <https://doi.org/10.3389/fncel.2022.886033>
- Ellenbroek, B., & Youn, J. (2016). Rodent models in neuroscience research: Is it a rat race? *Disease Models & Mechanisms*, 9(10), 1079-1087. <https://doi.org/10.1242/dmm.026120>
- Gao, S., Bell, E. C., Zhang, Y., & Liang, D. (2021). Racial disparity in drug disposition in the digestive tract. *International Journal of Molecular Sciences*, 22(3), 1038. <https://doi.org/10.3390/ijms22031038>
- Gökçek-Saraç, Ç., Karakurt, S., Adalı, O., & Jakubowska-

- Doğru, E. (2012). Correlation between hippocampal levels of neural, epithelial, and inducible NOS and spatial learning skills in rats. *Behavioral Brain Research*, 233(2), 493-499. <https://doi.org/10.1016/j.bbr.2012.08.005>
- Gökçek-Saraç, Ç., Wesierska, M., & Jakubowska-Doğru, E. (2015). Comparison of spatial learning in the partially baited radial-arm maze task between commonly used rat strains: Wistar, Sprague-Dawley, Long-Evans, and outcrossed Wistar/Sprague-Dawley. *Learning and Behavior*, 43(1), 83-94. <https://doi.org/10.3758/s13420-014-0163-9>
- Guitar, N. A., & Roberts, W. A. (2015). The interaction between working and reference spatial memories in rats on a radial maze. *Behavioral Processes*, 112, 100-107. <https://doi.org/10.1016/j.beproc.2014.10.007>
- Guo, X., Asthana, P., Zhai, L., Cheng, K. W., Gurung, S., Huang, J., Wu, J., Zhang, Y., Mahato, A. K., Saarma, M., Ustav, M., Kwan, H. Y., Lyu, A., Chan, K. M., Xu, P., Bian, Z. X., & Wong, H. L. X. (2024). Artesunate treats obesity in male mice and non-human primates through GDF15/GFRAL signalling axis. *Nature Communication*, 3;15(1):1034. <https://doi.org/10.1038/s41467-024-45452-3>
- Harker, T. K., & Whishaw, I. Q. (2002). Place and matching-to-place spatial learning affected by rat inbreeding (Dark-Agouti, Fischer 344) and albinism (Wistar, Sprague-Dawley) but not domestication (wild rat vs. Long-Evans, Fischer-Norway). *Behavioral Brain Research*, 134(1), 467-477. [https://doi.org/10.1016/s0166-4328\(02\)00083-9](https://doi.org/10.1016/s0166-4328(02)00083-9)
- Jaramillo, S., & Zador, A. M. (2014). Mice and rats achieve similar levels of performance in an adaptive decision-making task. *Frontiers in Systems Neuroscience*, 8, 173. <https://doi.org/10.3389/fnsys.2014.00173>
- Junttila, S., Valros, A., Mäki, K., Väättäjä, H., Reunanen, E., & Tiira, K. (2022). Breed differences in social cognition, inhibitory control, and spatial problem-solving ability in the domestic dog (*Canis familiaris*). *Scientific Reports*, 12(1), 22529. <https://doi.org/10.1038/s41598-022-26991-5>
- Kohler, J., Mei, J., Banneke, S., Winter, Y., Endres, M., & Emmrich, J. V. (2022). Assessing spatial learning and memory in mice: Classic radial maze versus a new animal-friendly automated radial maze allowing free access and not requiring food deprivation. *Frontiers in Behavioral Neuroscience*, 16, 1013624. <https://doi.org/10.3389/fnbeh.2022.1013624>
- Kovarova, V., Bordes, J., Mitra, S., Narayan, S., Springer, M., Brix, L. M., Deussing, J. M., & Schmidt, M. V. (2025). Deep phenotyping reveals CRH and FKBP51-dependent behavioral profiles following chronic social stress exposure in male mice. *Neuropsychopharmacology*, 50(3):556-567. <https://doi.org/10.1038/s41386-024-02008-9>
- Lee, J. W., & Jung, M. W. (2025). Memory consolidation from a reinforcement learning perspective. *Frontiers in Computational Neuroscience*, 8;18:1538741. <https://doi.org/10.3389/fncom.2024.1538741>
- Manahan-Vaughan, D., & Schwegler, H. (2011). Strain-dependent variations in spatial learning and in hippocampal synaptic plasticity in the dentate gyrus of freely behaving rats. *Frontiers in Behavioral Neuroscience*, 7, 5-7. <https://doi.org/10.3389/fnbeh.2011.00007>
- Manukyan, P., Romanova, E., Latanov, A., Shlepnev, P., Sharapkova, A., Garabova, N., et al. (2025). Challenges and insights of transferring animal maze studies principles to human spatial learning research. *Scientific Reports*, 15(1), 2096. <https://doi.org/10.1038/s41598-025-86037-4>
- McQuail, J. A., Dunn, A. R., Stern, Y., Barnes, C. A., Kempermann, G., Rapp, P. R., Kaczorowski, C. C., & Foster, T. C. (2021). Cognitive reserve in model systems for mechanistic discovery: the importance of longitudinal studies. *Frontiers in Aging Neuroscience*, 12, 607685. <https://doi.org/10.3389/fnagi.2020.607685>
- Nollen, N. L., Ahluwalia, J. S., Sanderson Cox, L., Okuyemi, K., Lawrence, D., Samuels, L., & Benowitz, N. L. (2021). Assessment of Racial Differences in Pharmacotherapy Efficacy for Smoking Cessation: Secondary Analysis of the EAGLES Randomized Clinical Trial. *JAMA Network Open*, 4(1), e2032053. <https://doi.org/10.1001/jamanetworkopen.2020.32053>
- Peleh, T., Ike, K. G. O., Wams, E. J., Lebois, E. P., & Hengerer, B. (2019). The reverse translation of a quantitative neuropsychiatric framework into preclinical studies: Focus on social interaction and behavior. *Neuroscience & Biobehavioral Reviews*, 97, 96-111. <https://doi.org/10.1016/j.neubiorev.2018.07.018>
- Ramos, J. M. (2000). Influence of the shape of the experimental room on spatial learning in rats. *Physiology & Behavior*, 70(3), 351-357. [https://doi.org/10.1016/s0031-9384\(00\)00266-3](https://doi.org/10.1016/s0031-9384(00)00266-3)
- Russomanno, G., Sison-Young, R., Livoti, L. A., Coghlan, H., Jenkins, R. E., Kunnen, S. J., Fisher, C. P., Reddyhoff, D., Gardner, I., Rehman, A. H., Fenwick, S. W., Jones, A. R., Vermeil De Conchard, G., Simonin, G., Bertheux, H., Weaver, R. J., Johnson, R. L., Liguori, M. J., Clausznitzer, D., Stevens, J. L., & Copple, I. M. (2023). A systems approach reveals species differences in hepatic stress response capacity. *Toxicological Science: An Official Journal of the Society of Toxicology*, 196(1), 112-125. <https://doi.org/10.1093/toxsci/kfad085>
- Sarmiento, L. F., Lopes da Cunha, P., Tabares, S., Tafet, G., & Gouveia, A. J. (2024). Decision-making under stress: A psychological and neurobiological integrative model. *Brain, Behavior, and Immunity - Health*, 38, 100766. <https://doi.org/10.1016/j.bbih.2024.100766>
- Sitnikova, E. (2024). Behavioral and Cognitive Comorbidities in Genetic Rat Models of Absence Epilepsy (Focusing on GAERS and WAG/Rij Rats). *Biomedicine*, 7;12(1):122. <https://doi.org/10.3390/biomedicine12010122>
- Vorhees, C. V., Williams, M. T. (2024). Tests for learning and memory in rodent regulatory studies. *Current Research in Toxicology*, 18;6:100151. <https://doi.org/10.1016/j.crtox.2024.100151>
- Wijnen, K., Genzel, L., & van der Meij, J. (2024). Rodent maze studies: From following simple rules to complex map learning. *Brain Structure and Function*, 229(4), 823-841. <https://doi.org/10.1007/s00429-024-02771-x>