

Impact of Experimental Diabetes on Memory Performance in Mice

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How to cite this paper: Doubran, P.J.D., Begbin, K.E., Kanga, A.J. and Tako, N.A. (2026) Impact of Experimental Diabetes on Memory Performance in Mice. *Journal of Biosciences and Medicines*, **14**, 216-226. <https://doi.org/10.4236/jbm.2026.147018>

Received: June 13, 2026

Accepted: July 14, 2026

Published: July 17, 2026

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Abstract

Diabetes mellitus is a major public health problem due to its global spread and the severity of its complications, particularly cognitive impairment, which affects life expectancy and quality of life. The aim of this study was to evaluate the effect of alloxan-induced experimental diabetes on memory performance in mice. The study was conducted on adult male mice aged 12 to 14 weeks, weighing between 28 and 33 g, divided into a diabetic group and a non-diabetic control group. Diabetes was induced by a single intraperitoneal injection of alloxan (220 mg/kg). Blood glucose levels and body weight were measured weekly over the four weeks of the experiment. Spatial memory was assessed using the T-maze test according to the spontaneous alternation method. Diabetic mice showed severe and persistent hyperglycemia and significant progressive weight loss compared to controls. The memory performance of diabetic mice declined progressively, with the alternation rate falling from $81.05 \pm 1.61\%$ to $60.52 \pm 1.96\%$ over four weeks, while the control group remained stable at around $83.68 \pm 1.99\%$ and $85.79 \pm 1.12\%$. The differences between groups were significant ($p < 0.05$) from the first week and highly significant from the second week onwards ($p < 0.001$). Alloxan-induced experimental diabetes significantly impairs spatial memory in mice, confirming the link between diabetes mellitus and cognitive deficits.

Keywords

Diabetes, Spatial Memory, Cognitive Impairment, T-Maze

1. Introduction

Diabetes mellitus is a major public health problem due to its global spread, the

severity of its complications, which affect life expectancy and quality of life, and the excessive costs it generates, which place a strain on the budgets of the poorest countries [1]. It is generally classified as type 1 diabetes (T1D) and type 2 diabetes (T2D). T1D is an autoimmune disease characterized by a defect in the secretion of endogenous insulin by the pancreas [2] [3]. It manifests as high blood glucose levels, causing regular episodes of hypoglycemia and hyperglycemia that require regular self-monitoring and daily insulin administration [4]. In 2024, approximately 9.2 million people worldwide, including 7.4 million under the age of 20, were living with T1D [5]. The main goal of diabetes mellitus management is to restore glycemic balance in order to prevent complications [6]. Among these complications, cognitive dysfunction is a major concern due to its potential impact on patients' quality of life and independence [7]. However, most studies on the link between chronic hyperglycemia and cognitive impairment focus on T2D [8]. This is because the population living with T2D is growing [9] [10]. Furthermore, the management of T2D in this population poses particular problems [11] [12]. Furthermore, among the various conditions associated with T2D, cognitive frailty plays an important role because it directly impacts adherence to any proposed treatment and promotes medication errors, especially given the high frequency of polypharmacy in this population [13]. One of the factors put forward to explain this problem is that T2D occurs mainly in older people, since age is also a risk factor for cognitive impairment [14] [15]. In this context, it seems necessary to continue research on T1D in order to better understand, in a comprehensive manner, the links between diabetes mellitus and cognitive impairment.

Animal models, particularly mice, provide a better understanding of the biological mechanisms involved in these cognitive deficits because the murine and human genomes are relatively similar in structure [16]. Furthermore, the induction of experimental diabetes, usually by alloxan, reproduces several metabolic characteristics of human type 1 diabetes [17]. It is therefore essential to evaluate the effects of experimental diabetes on spatial memory in order to better understand the mechanisms involved and identify possible therapeutic avenues. The present study is part of this effort and aims to evaluate the impact of alloxan-induced diabetes on spatial memory performance in mice.

2. Materials and Methods

2.1. Experimental Animals

This study was conducted on adult male mice (*Mus musculus* Linnaeus, 1758) of the Swiss strain, aged 12 to 14 weeks and weighing between 28 and 33 g. These animals came from the vivarium of the École Normale Supérieure Abidjan (Côte d'Ivoire). They were kept at a constant temperature of 27 to 29°C, relative humidity of 65%, and 12-hour light/dark cycles. They were fed and watered *ad libitum* throughout the experiment. The animals used in this study were treated in accordance with the ethical principles of the Canadian Council on Animal Care regarding the use of animals in science.

2.2. Technical Equipment

The technical equipment consisted mainly of 98% alloxan monohydrate supplied by Polychimie (Abidjan, Côte d'Ivoire), a glucometer with test strips (On Call® Extra, San Diego, United States) for measuring blood glucose levels, insulin syringes (BD Micro-Fine, France) for intraperitoneal injections of the alloxan solution, and a T-maze. The latter is made of gray Plexiglas. The T-maze was designed according to the model described by Badjo *et al.* [18]. It consists of a starting compartment ($15 \times 10 \times 22$), a central corridor ($45 \times 10 \times 22$), and two identical exit arms ($31 \times 10 \times 22$). Access to each compartment can be closed using a system of side-sliding guillotine doors.

2.3. Diabetes Induction and Experimental Design

Diabetes induction follows the protocol described by Bégbin *et al.* [19]. A total of 32 mice were included in the study. Of these, 22 underwent diabetes induction, while 10 made up the healthy control group. After a 16-hour fast imposed on all animals, the mice in the experimental group received a single intraperitoneal injection of alloxan at a dose of 220 mg/kg body weight, dissolved in isotonic saline (0.9% NaCl). The control mice received, under the same conditions, an equivalent volume of pure saline solution.

Hyperglycemia developed three days after alloxan administration. One week after induction, blood glucose levels were measured to validate the model: only mice with blood glucose levels above 300 mg/dL were considered diabetic. Of the 22 treated mice, 4 that did not reach this threshold and 8 that died were excluded from the study. The remaining 10 diabetic mice and the 10 control mice were divided into two groups of 10 animals each:

- 1) the diabetic group;
- 2) the non-diabetic control group.

The animals' cognitive performance was then assessed using the T-maze test. This assessment took place over a four-week period, beginning one week after the induction of diabetes (with week 0 corresponding to the first day of the behavioral test). At the same time, fasting blood glucose levels and body weight were measured weekly.

2.4. T-Maze Test

Spontaneous alternations are assessed using the method described by Doubran *et al.*, which includes a habituation phase, a pre-test session, and then the test session itself [20].

- 1) Habituation phase

The mice are first subjected to two habituation sessions of ten minutes each (one per day), during which they freely explore the entire maze. This step aims to familiarize them with the environment and reduce stress related to novelty.

- 2) Pre-test session

The animals then undergo an initial session of sequential alternations designed

to accustom them to the experimental procedure (confinement, opening and closing of doors, handling). This also helps to establish the alternating behavior, as repeated exploration contributes to the development of a spatial representation of the device. This session consists of five consecutive trials, separated by a 30-second inter-trial interval (ITI).

3) Test session

The next day, the test phase takes place, consisting of twenty (20) consecutive trials, each separated by a 30-second ITI. In each trial, the animal is first held in the starting compartment for 30 seconds. The door is then opened and the animal is free to choose one of the two arrival arms, in which it remains confined for 30 seconds. It is then returned to the starting compartment for 30 seconds before the next trial. The experiment was conducted over four weeks at a rate of one T-maze test per week.

4) Measured parameters

A point is awarded when the animal chooses a different arm from the one selected in the previous trial; otherwise, the trial is scored as 0. The percentage of spontaneous alternation (AS%) over all 20 trials is obtained by the ratio between the number of alternations achieved (NAP) and the number of possible alternations (NPA) multiplied by one hundred.

2.5. Statistical Analysis

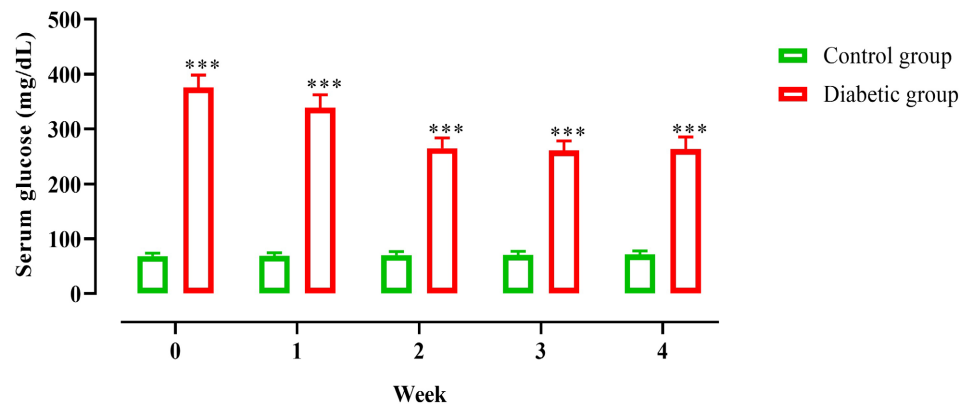
Data are presented as the mean $\pm$ standard error of the mean ($M \pm SEM$). Statistical analyses were performed using GraphPad Prism 8.0.1 software (San Diego, California, United States). Comparisons between the diabetic group and the control group were performed separately for each week of follow-up using a Student's t-test for independent samples. This approach was chosen because the objective was to compare the two groups at each measurement time point, independently of the other weeks, rather than to analyze the longitudinal changes in the same animals over time. Differences were considered statistically significant at a p-value < 0.05 .

3. Results

3.1. Blood Glucose Levels in Mice

A significant and consistent difference was observed between the blood glucose levels of diabetic mice and non-diabetic mice throughout the experiment (**Figure 1**). From week zero, diabetic mice had very high blood glucose levels (379.2 ± 6.39 mg/dL) compared to non-diabetic mice (68.6 ± 1.69 mg/dL), representing a highly significant increase ($p < 0.001$) of more than 450%. In week one, diabetic mice maintained blood glucose levels well above normal (333.7 ± 7.85 mg/dL), while non-diabetic mice remained stable at 71.5 ± 2.00 mg/dL. The 366.7% increase in blood glucose levels remains highly significant ($p < 0.001$). This trend is also observed in weeks two and three, where blood glucose levels increase by 280.5% and 275.3%, respectively. In the final week (week 4), diabetic mice still had very high

blood glucose levels (259.9 ± 7.26 mg/dL), compared to 71.0 ± 1.41 mg/dL for non-diabetic mice, a difference of 266%. This increase remains highly significant ($p < 0.001$).

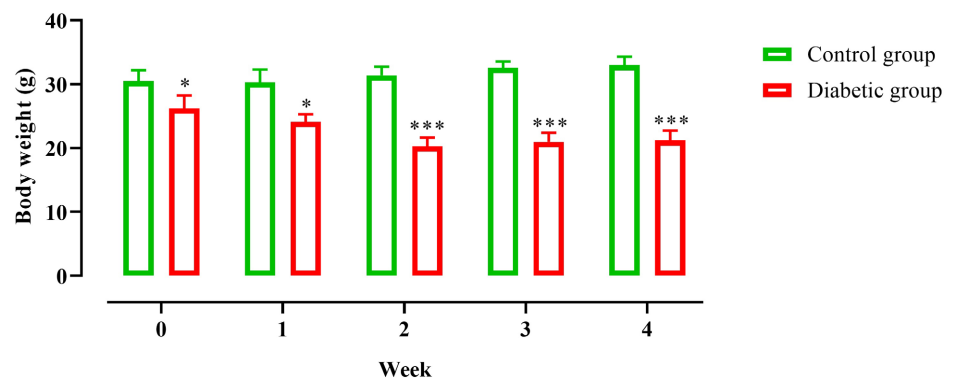


Note: Data are presented as mean $\pm$ SEM and analyzed by the Student's t-test. * $p < 0.05$, ** $p < 0.01$ *** $p < 0.001$ compared to the control ($n = 10$).

Figure 1. Changes in blood glucose levels in mice during the experiment.

3.2. Body Mass of Mice

Figure 2 shows a clear and gradual decrease in body mass in diabetic mice compared to non-diabetic mice, which gained slightly in weight throughout the experiment. In fact, a significant difference was already apparent in week 0. Diabetic mice had an average body mass of 25.6 ± 0.50 g compared to 30.5 ± 0.54 g for non-diabetic mice, a reduction of more than 16% ($p < 0.05$). In the first week, weight loss continued in diabetic mice, which reached 23.9 ± 0.35 g. The gap widened to more than 21% and remained significant ($p < 0.05$). This decline became more pronounced in weeks 2 and 3 (33.75% and 36.19%). Finally, in the fourth week, diabetic mice still had a significantly lower weight (21.5 ± 0.34 g) compared to non-diabetic mice (33 ± 0.42 g), representing a highly significant ($p < 0.001$) decrease of nearly 34%.

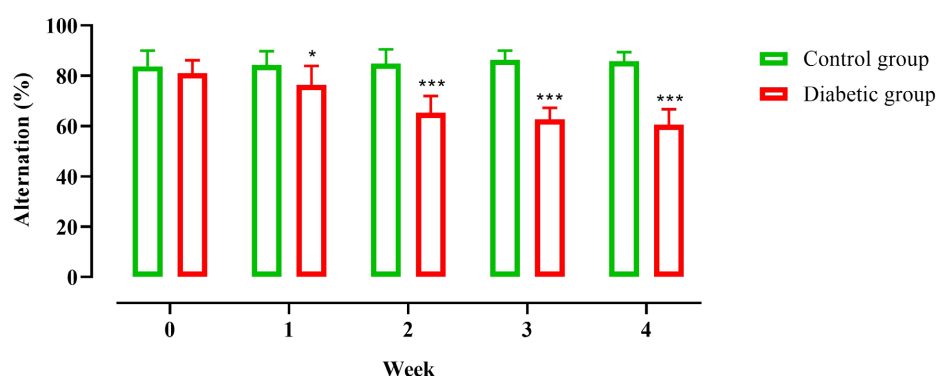


Note: Data are presented as mean $\pm$ SEM and analyzed by the Student's t-test. * $p < 0.05$, ** $p < 0.01$ *** $p < 0.001$ compared to the control ($n = 10$).

Figure 2. Change in body mass of mice during the experiment.

3.3. Memory Performance of Mice in the T-Maze Test

A gradual and significant decline in memory performance was observed in diabetic mice over the course of several weeks (Figure 3). At week zero, both groups showed similar spontaneous alternation rates, with $83.68 \pm 1.99\%$ for non-diabetic mice and $81.05 \pm 1.61\%$ for diabetic mice; no statistically significant difference was observed ($p = 0.317$). From the first week onwards, an initial decrease appeared in diabetic mice, whose alternation rate fell to $76.31 \pm 2.38\%$, compared to $84.21 \pm 1.75\%$ in the controls, indicating a significant difference ($p = 0.015$). This decrease became more pronounced in the second week, when diabetic mice showed only $65.26 \pm 2.11\%$ alternations, while non-diabetic mice remained stable at $84.74 \pm 1.83\%$. The difference reached 19.48% and became highly significant ($p < 0.001$). The trend continued in the third week, when diabetic mice fell to $62.63 \pm 1.46\%$, compared to $86.31 \pm 1.16\%$ for the controls, a marked and significant difference ($p < 0.001$). Finally, in the fourth week, the performance of diabetic mice reached its lowest level ($60.52 \pm 1.96\%$), while non-diabetic mice maintained a rate of $85.79 \pm 1.12\%$, representing an equally significant reduction ($p < 0.001$) of 25.27%.



Note: Data are presented as mean $\pm$ SEM and analyzed by the Student's t-test. * $p < 0.05$, ** $p < 0.01$ *** $p < 0.001$ compared to the control ($n = 10$).

Figure 3. Evolution of spontaneous alternations in the T-maze test in diabetic mice compared to non-diabetic mice over a four-week period.

4. Discussion

Diabetic mice exhibited severe and persistent hyperglycemia and significant progressive weight loss compared to controls throughout the T-maze tests. Results similar to ours also describe a marked and sustained increase in blood glucose levels in mice given alloxan [21] or streptozotocin [22], confirming the ability of these substances to cause profound pancreatic destruction and stable metabolic imbalance. Similarly, the study by Kumar and Sharma on alloxan-induced diabetic neuropathy reports persistent hyperglycemia in untreated mice, as well as a progressive deterioration in general health, reflected in particular by a decrease in body weight [23]. These observations indicate that the results obtained in our T-maze test are closely related to alloxan-induced experimental diabetes.

The results of the T-maze test show a progressive and significant decrease in

memory performance in diabetic mice, observed from the first week to the fourth week. This decline in spontaneous alternation reflects a growing deficit in spatial working memory, which is a primary function of the hippocampus and frontal regions. The widening gap between diabetic mice and controls suggests that chronic hyperglycemia has cumulative deleterious effects on the neural circuits involved in spatial memory.

These results are consistent with a series of recent studies on the effects of experimental diabetes on cognitive function. Indeed, mouse models of diabetes, whether induced by alloxan [24], streptozotocin [25] or related to metabolic predispositions [26] [27], systematically develop deficits in working memory and spatial memory. This research indicates that chronic hyperglycemia creates a neurotoxic environment. Indeed, it has been shown that chronic diabetes alters neuronal plasticity and activates inflammatory pathways responsible for cognitive deficits [28]. In addition, chronic hyperglycemia promotes ferroptosis of hippocampal neurons, a mechanism of cell death that exacerbates memory disorders [29]. More recently, Li *et al.* showed that high concentrations of β -hydroxybutyrate (β -OHB) in diabetic mouse models disrupt the α subunit of CaMKII- α (calcium/calmodulin-dependent kinase II- α) in the hippocampus, which could contribute to memory deficits in T1D mice [30]. Furthermore, a previous study described a progressive worsening of spatial memory deficits proportional to the duration of exposure to hyperglycemia in their work on time-dependent alterations in learning and memory in streptozotocin-induced hyperglycemic rats [31]. This phenomenon is perfectly consistent with the results we obtained in our study.

However, it is interesting to note that interventions can mitigate these cognitive deficits in diabetic mice. Indeed, aerobic exercise could increase the expression of MALAT1 (Metastasis-Associated Lung Adenocarcinoma Transcript 1) in exosyl-serums to competitively inhibit miR-382-3p and increase BDNF (Brain-Derived Neurotrophic Factor) expression, thereby improving cognitive impairment in mice with type 2 diabetes [32]. Furthermore, Nan *et al.* demonstrated in diabetic ovariectomized mice, in which cognitive impairment is more severe, that forsythoside B could be a new therapeutic target for the treatment of postmenopausal diabetic encephalopathy [33].

Clinical data in humans confirm our findings. Diabetic patients, particularly those with hypertensive comorbidity, have an increased prevalence of cognitive impairment [34]. Diabetes has also been shown to interact with markers of cerebral vascular disease to accelerate cognitive decline and increase the risk of dementia [35]. The findings of Lu *et al.* clarify that it is not only chronic hyperglycemia that is harmful, but also glycemic variability [36]. This is associated with morphological changes in the brain and reduced cognitive performance. At the neuropsychological level, diabetes-related disorders preferentially affect certain cognitive domains such as attention and executive functions [37]. In addition, Satapathy *et al.* have shown that microvascular complications are a major factor in cognitive decline through impaired cerebral perfusion and neuroinflammatory mechanisms [38]. These mechanisms could contribute to the progressive deterio-

ration in memory performance observed in our diabetic mice. Similarly, it has been reported that even the early stages of cognitive impairment in diabetic patients are accompanied by disturbances affecting memory, attention, and learning [39] [40]. Finally, the summary proposed by Kan *et al.* reminds us that diabetes mellitus is a major and independent risk factor for cognitive decline, through a set of mechanisms including oxidative stress, advanced glycation, inflammation, and vascular damage [41].

Ultimately, this study shows that the alloxan-induced mouse model of diabetes effectively replicates the metabolic alterations and early working memory deficits associated with chronic hyperglycemia. This model thus serves as a valuable tool for exploring the mechanisms involved in diabetes-related cognitive impairments, including oxidative stress, neuroinflammation, alterations in synaptic plasticity, and neuronal death. However, findings from mouse studies do not allow for direct conclusions about the mechanisms of cognitive decline in humans, which results from complex interactions between metabolic, vascular, genetic, environmental, and age-related factors. Thus, although this model provides valuable insights into the biological mechanisms potentially involved, clinical and translational studies remain essential to confirm their role in human cognitive decline and assess their therapeutic relevance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Jaffiol, C. (2021) Le diabète en 2021: Progrès, échecs et perspectives. *Bulletin de l'Académie des Sciences et Lettres de Montpellier*, **52**, 1-14.
- [2] Morgan, N.G. (2024) Insulinitis in Human Type 1 Diabetes: Lessons from an Enigmatic Lesion. *European Journal of Endocrinology*, **190**, R1-R9.
<https://doi.org/10.1093/ejendo/lvae002>
- [3] Cheng, R. (2025) La prévention de l'hypoglycémie non sévère avec des glucides oraux à un seuil glycémique plus élevé que celui établi dans les recommandations actuelles chez les adultes atteints de diabète de type 1. Mémoire de Maîtrise, Université de Montréal, 111 p.
<https://umontreal.scholaris.ca/items/6612b997-e7cc-4640-a3cb-b471f1021234>
- [4] Vinel, V., Diasio, N. and Bichet, L. (2021) Enfants et adolescents face à la maladie chronique: Le cas du diabète de type 1. *Revue des Politiques Sociales et Familiales*, **138**, 89-97.
- [5] International Diabetes Federation (2025) Atlas du diabète de la FID (11e éd.). IDF.
<https://idf.org/fr/news-and-resources/resources/idf-diabetes-atlas-11th-edition-2025/>
- [6] Dimore, A.L., Edosa, Z.K. and Mitiku, A.A. (2023) Glycemic Control and Diabetes Complications among Adult Type 2 Diabetic Patients at Public Hospitals in Hadiya Zone, Southern Ethiopia. *PLOS ONE*, **18**, e0282962.
<https://doi.org/10.1371/journal.pone.0282962>
- [7] Julla, J.B., Vidal-Trecan, T., Dumurgier, J., Paquet, C., Mersel, H., Gautier, J.F., *et al.*

- (2021) Étude des déterminants des fonctions cognitives chez les patients diabétiques de type 1 adultes. *Annales d'Endocrinologie*, **82**, 338 p.
<https://doi.org/10.1016/j.ando.2021.08.230>
- [8] Sola, T., Sola, F.M. and Jehkonen, M. (2024) The Effects of Type 2 Diabetes on Cognitive Performance: A Review of Reviews. *International Journal of Behavioral Medicine*, **31**, 944-958. <https://doi.org/10.1007/s12529-024-10274-6>
- [9] Guzman-Vilca, W.C. and Carrillo-Larco, R.M. (2024) Number of People with Type 2 Diabetes Mellitus in 2035 and 2050: A Modelling Study in 188 Countries. *Current Diabetes Reviews*, **21**, 1-8. <https://doi.org/10.2174/0115733998274323231230131843>
- [10] American Diabetes Association Professional Practice Committee (2024) Older Adults: Standards of Care in Diabetes—2024. *Diabetes Care*, **47**, 244-257.
- [11] Godman, B., Basu, D., Pillay, Y., Mwita, J.C., Rwegerera, G.M., Anand Paramadhas, B.D., *et al.* (2020) Review of Ongoing Activities and Challenges to Improve the Care of Patients with Type 2 Diabetes across Africa and the Implications for the Future. *Frontiers in Pharmacology*, **11**, Article ID: 108.
<https://doi.org/10.3389/fphar.2020.00108>
- [12] Diyane, K., El Ansari, N., El Mghari, G., Anzid, K. and Cherkaoui, M. (2013) Caractéristiques de l'association diabète type 2 et hypertension artérielle chez le sujet âgé de 65 ans et plus. *Pan African Medical Journal*, **14**, Article 100.
- [13] Sugimoto, T., Arai, H. and Sakurai, T. (2021) An Update on Cognitive Frailty: Its Definition, Impact, Associated Factors and Underlying Mechanisms, and Interventions. *Geriatrics & Gerontology International*, **22**, 99-109.
<https://doi.org/10.1111/ggi.14322>
- [14] Liu, G., Li, Y., Xu, Y. and Li, W. (2022) Type 2 Diabetes Is Associated with Increased Risk of Dementia, but Not Mild Cognitive Impairment: A Cross-Sectional Study among the Elderly in Chinese Communities. *Frontiers in Aging Neuroscience*, **14**, Article ID: 1004954. <https://doi.org/10.3389/fnagi.2022.1004954>
- [15] Beck, E. and Scheen, A. (2025) Comment je traite... la gestion du diabète de type 2 chez la personne âgée. *Revue Médicale de Liège*, **80**, 73-79.
<https://pubmed.ncbi.nlm.nih.gov/39950520/>
- [16] Guillaudeux, N. (2021) Comparer des structures de gènes pour la prédiction de transcrits alternatifs codants chez l'humain, la souris et le chien. Autre [cs.OH]. Thèse de Doctorat, Université de Rennes.
- [17] Kim, J. (2024) Induction of Diabetes Mellitus Using Alloxan in Sprague Dawley Rats. *Cureus*, **16**, 1-8. <https://doi.org/10.7759/cureus.63359>
- [18] Badjo, P., Diboh, E., Gbalou, K.L., Adou, K.F.J., Zunon-Kipre, I. and Tako, N.A. (2017) Effets d'une consommation prolongée de «Koutoukou» (Boisson alcoolique artisanale) sur la mémoire spatiale chez la souris. *Journal of Applied Biosciences*, **116**, 11557-11565. <https://doi.org/10.4314/jab.v11i6.4>
- [19] Bégbin, K.E., Zougrou, N.E., Abizi, G., Kouakou, K. and Jaurès Mangué, N.E. (2021) Effects of Diabetes Mellitus on the Reproductive System of Adult Male Mice after One Cycle of Spermatogenesis. *European Scientific Journal ESJ*, **17**, 149-161.
<https://doi.org/10.19044/esj.2021.v17n34p149>
- [20] Doubran, P.J.D., Yao, K.M. and Ouattara, N. (2020) Effets comparés du traitement à l'alcool des ratte gestantes *et* allaitantes sur les performances mnésiques de leurs progénitures. *International Journal of Biological and Chemical Sciences*, **14**, 2028-2036. <https://doi.org/10.4314/ijbcs.v14i6.8>
- [21] Etti, I.C., Essang, E.A. and Olorunsola, E.O. (2024) Potential Effect of Chloroquine

- in Modulating Hyperglycemia and PTEN Receptor Linked Dyslipidemia on Alloxan-Induced Diabetic Mice. *Asian Journal of Biochemistry, Genetics and Molecular Biology*, **16**, 62-69. <https://doi.org/10.9734/ajbgmb/2024/v16i6383>
- [22] Wang, L.P., Geng, J., Liu, C., Wang, Y., Zhang, Z. and Yang, G.Y. (2022) Diabetes Mellitus-Related Neurobehavioral Deficits in Mice Are Associated with Oligodendrocyte Precursor Cell Dysfunction. *Frontiers in Aging Neuroscience*, **14**, Article ID: 846739.
- [23] Kumar, R. and Sharma, A.K. (2022) Effect of Teneligliptin, and Teneligliptin Combined with Gabapentin on Alloxan-Induced Diabetic Neuropathy in Albino Mice. *Asian Pacific Journal of Health Sciences*, **9**, 167-174. <https://doi.org/10.21276/apjhs.2022.9.4s1.30>
- [24] Keletela, J.I.A., Loubano-Voumbi, G., Miguel, L.M., Tchatchouang Njilo, D.G., Mboungou Malonga, A.M.E., Pouki, F.S., *et al.* (2024) Study of Cognitive Associated with Diabetes Induced by Alloxane Monohydrate in Wistar Rats. *European Journal of Medical and Health Research*, **2**, 236-244. [https://doi.org/10.59324/ejmhr.2024.2\(6\).32](https://doi.org/10.59324/ejmhr.2024.2(6).32)
- [25] Janthakhin, Y., Juntapremjit, S., Hummel, K., Razzazi-Fazeli, E. and Kingtong, S. (2024) The Alteration of Proteomic Profiles in Hippocampus of Type 2 Diabetic Mice Associated with Cognitive Impairment. *Bioinformatics and Biology Insights*, **18**, 1-13. <https://doi.org/10.1177/11779322241306290>
- [26] Carús-Cadavieco, M., Berenguer López, I., Montoro Canelo, A., Serrano-Lope, M.A., González-de la Fuente, S., Aguado, B., *et al.* (2023) Cognitive Decline in Diabetic Mice Predisposed to Alzheimer's Disease Is Greater than in Wild Type. *Life Science Alliance*, **6**, e202201789. <https://doi.org/10.26508/lsa.202201789>
- [27] Ab-Hamid, N., Omar, N., Ismail, C.A.N. and Long, I. (2023) Diabetes and Cognitive Decline: Challenges and Future Direction. *World Journal of Diabetes*, **14**, 795-807. <https://doi.org/10.4239/wjd.v14.i6.795>
- [28] Piątkowska-Chmiel, I., Gawrońska-Grzywacz, M., Popiolek, Ł., Herbet, M. and Dudka, J. (2022) The Novel Adamantane Derivatives as Potential Mediators of Inflammation and Neural Plasticity in Diabetes Mice with Cognitive Impairment. *Scientific Reports*, **12**, Article No. 6708. <https://doi.org/10.1038/s41598-022-10187-y>
- [29] Wang, B., Zhu, S., Guo, M., Ma, R., Tang, Y., Nie, Y., *et al.* (2024) Artemisinin Ameliorates Cognitive Decline by Inhibiting Hippocampal Neuronal Ferroptosis via NRF2 Activation in T2DM Mice. *Molecular Medicine*, **30**, 1-14. <https://doi.org/10.1186/s10020-024-00797-9>
- [30] Li, H., Chen, R., Wang, H., Tian, J., Zhao, Y. and Cen, X. (2025) Hippocampal Camkii- α β -Hydroxybutyrylation Induces Memory Deficits in Mice with Type 1 Diabetes Mellitus. *Communications Biology*, **8**, 1-15. <https://doi.org/10.1038/s42003-025-08832-z>
- [31] Ahmed, A., Zeng, G., Jiang, D., Lin, H., Azhar, M., Farooq, A.D., *et al.* (2019) Time-dependent Impairments in Learning and Memory in Streptozotocin-Induced Hyperglycemic Rats. *Metabolic Brain Disease*, **34**, 1431-1446. <https://doi.org/10.1007/s11011-019-00448-7>
- [32] Wang, M., Xie, K., Zhao, S., Jia, N., Zong, Y., Gu, W., *et al.* (2023) Aerobic Exercise Improves Cognitive Impairment in Mice with Type 2 Diabetes by Regulating the MA-LAT1/miR-382-3p/BDNF Signaling Pathway in Serum-Exosomes. *Molecular Medicine*, **29**, 1-23. <https://doi.org/10.1186/s10020-023-00727-1>
- [33] Nan, X., Sun, Q., Xu, X., Yang, Y., Zhen, Y., Zhang, Y., *et al.* (2022) Forsythoside B Ameliorates Diabetic Cognitive Dysfunction by Inhibiting Hippocampal Neuroin-

- inflammation and Reducing Synaptic Dysfunction in Ovariectomized Mice. *Frontiers in Aging Neuroscience*, **14**, Article ID: 974690. <https://doi.org/10.3389/fnagi.2022.974690>
- [34] Liu, H., Feng, Z., Zhang, W., Liu, Y., Xiong, N., Chen, W., *et al.* (2024) Prevalence of Cognitive Impairment and Its Associated Factors in Type 2 Diabetes Mellitus Patients with Hypertension in Hunan, China: A Cross-Sectional Study. *Frontiers in Psychiatry*, **15**, Article ID: 1445323. <https://doi.org/10.3389/fpsyt.2024.1445323>
- [35] Cui, J., Robert, C., Teh, C.M., Jun Yi, E.C., Chong, J.R., Tan, B.Y., *et al.* (2024) Interactive Effect of Diabetes Mellitus and Subclinical MRI Markers of Cerebrovascular Disease on Cognitive Decline and Incident Dementia: A Memory-Clinic Study. *Alzheimer's Research & Therapy*, **16**, Article No. 214. <https://doi.org/10.1186/s13195-024-01577-7>
- [36] Lu, W., Shen, D. and Qiu, S. (2025) Association between Visit-to-Visit Glucose Variability and Brain Morphology and Cognitive Function in Type 2 Diabetes. *The Journal of Clinical Endocrinology & Metabolism*, **110**, 3461-3469. <https://doi.org/10.1210/clinem/dgaf228>
- [37] Xiao, X., Chen, L., Liu, J., Cai, J. and Deng, M. (2025) Cognitive Domain-Specific Impairments and Associated Risk Factors in Type 2 Diabetes Mellitus: A Cross-Sectional Observational Study Based on Neuropsychological Assessment from Xiamen, China. *PeerJ*, **13**, e20292. <https://doi.org/10.7717/peerj.20292>
- [38] Satapathy, P., Pratima, P., Gaidhane, A.M., Vadia, N., Menon, S.V., *et al.* (2025) Prevalence and Impact of Microvascular Complications in Type 2 Diabetes Mellitus on Cognitive Impairment and Depression: A Systematic Review and Meta-Analysis. *Diabetology & Metabolic Syndrome*, **17**, Article No. 187.
- [39] Abdellatif, G.A., Hassan, A.M., Gabal, M.S., Hemeda, S.A., El-Chami, N.H. and Salama, I.I. (2020) Mild Cognitive Impairment among Type II Diabetes Mellitus Patients Attending University Teaching Hospital. *Open Access Macedonian Journal of Medical Sciences*, **8**, 105-111. <https://doi.org/10.3889/oamjms.2020.4245>
- [40] Reyes Bueno, J.A., Sánchez-Guijo, G., Ráez, P.D., García-Arnés, J.A., Garzón-Maldonado, F.J., Castro, V.S., *et al.* (2024) Effects of Type 2 Diabetes on the Neuropsychological Profile in Mild Cognitive Impairment. *Journal of Alzheimer's Disease*, **99**, 887-897. <https://doi.org/10.3233/jad-230791>
- [41] Kan, W., Qu, M., Wang, Y., Zhang, X. and Xu, L. (2025) A Review of Type 2 Diabetes Mellitus and Cognitive Impairment. *Frontiers in Endocrinology*, **16**, Article ID: 1624472. <https://doi.org/10.3389/fendo.2025.1624472>