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Building for the Mind A Neuro-Architectural Approach of Spatial Experience for Sustainable Mental Health and Wellbeing

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ABSTRACT

With the growing recognition of the significance of sustainable development and promoting good health and wellbeing, sustainable development and mental health are still newly integrated in the scientific literature. This research aims to highlight the potential of neuro-architecture, which is an interdisciplinary field that studies the relationship between the built environment, cognitive neuroscience and psychology, of enabling architects to gain more scientific-based studies to understand the biological and sensory effect of built environments on man's brain for sustainable mental health. This is a quantitative deductive experimental research adopting comparative neuroscientific approach to measure the impact of form of space boundaries on animal model where spatial experience created by form of space boundaries is the only changed parameter and the only variable. This is attained by conducting behavioural assessment and biological tests. Data are analysed statistically using ANOVA & Duncan's. Behaviour assessment using the Y-Maze test demonstrated that mice housed in a space with mixed formations of rectilinear and curvilinear boundaries had strong working memory that indicates intact prefrontal cortical performance. Also, biological tests results showed a significant increase in formation of antioxidants in the same space. These findings promote that incorporating curvilinear geometries into space not only have an aesthetic and psychological preference but also can have neurological enriching impact over a long period of time on brain health.

Practical implications

This research sheds light on the multidisciplinary approach of architecture and urban design. The science-based method adopted clarifies that architects and urban designers can seek evidence using scientific tools and including scientific approaches in design decisions. Creating inspiring spaces which affect users' moods, health and well-being can be easily verified using experimentation. Thus, sustainable design is not limited to applying surficial strategies, but also can be included into actual evaluation based on biological variations. Thus, sustainable architecture and wellbeing can be proven scientifically to inform architects and designers regarding a revolutionary approach in designing spaces.

Originality

The researchers confirm that this research is their original work, and that all the assistance received and resources have been acknowledged, and they are responsible for its content and authenticity.

Index-words: *Comparative Cognitive Neuroscience, Mental Health, Neuro-architecture, Organic architecture, Space Boundaries, Spatial Memory, Sustainable architecture, Oxidative stress.*

I. INTRODUCTION

Over the years, our senses and neural systems as biological beings have developed in response to our environmental demands. Architecture and the built environment, which constitute people everyday life experience, have a great impact on our wellbeing cognitively and emotionally. In this era of sustainable development, there is a quest for an evidence-based research approach towards sustainable designs for sustainable minds.

According to the United Nations meeting in 2015, improving good health and wellbeing comes third among the 17 Sustainable Development Goals (SGDs) referred to as the 2030 Agenda. Goal number three aims to 'ensure healthy lives and promote well-being for all at all ages'. In 1946, the World Health

Organisation (WHO) defined health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. Also, the WHO referred to mental health as 'the state of mental well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work well, and contribute to their community' [1]. Studies have proven that here is a direct connection between the immune system and the central nervous system where continuous psychological stress affects the immune system and triggers the formation of neuropsychiatric disorders and affects the overall health [2].

According to the WHO in 2022, around 55 million people around the world have dementia, a neuro-degenerative disorder associated with deficits in executive processes and overall cognitive wellbeing, this number is expected to reach 78 million in 2030 and 139 million in 2050 [3].

Individual differences in cognitive decline are caused by a combination of factors including genetics, sex, lifestyle, environmental factors [4] and stress [5] that interact to affect the structure and function of the brain system [6].

The European Academy of Neurology's (EAN) adopted a positive approach "one brain, one life, one approach" that aims to prevent neurological disorders and also aims to preserve brain health and promote brain recovery [7] as recent research suggests that nearly 40% of dementias are preventable [8].

The action plan adopted by the WHO 2013-2030 in the 'World Mental Health report: Transforming Mental Health for all' highlighted three 'Paths of Transformation' which are increasing the awareness of the importance of mental health, enhancing mental health services quality, and finally, reshaping the social, cultural, and physical characteristics of the surrounding environment in homes, schools and workplaces.

As one spends more than 80% of his/her life in built environments, and although there is rich literature on how architectural design parameters impact users' physical health including temperature, low-emission finishing materials, ventilation systems [9], humidity levels [10], noise control and proper lightening [11] [12] [13], it is still of great importance to investigate the impact of architectural spaces in which one lives on his/her neurological functioning and cognitive performance [14].

The continuous exposure to stressful environments can affect one's body psychophysiological mechanisms where chronic stress suppress the immune system leading to the feeling of chronic stress and fatigue [15]. This overtime affects both one's physical and mental wellbeing where continuous exposure to stressful urban and built environments increases the cognitive load on one's brains to process and affect one's mental well-being.

The Urbanization Development Studies conducted at the World Bank 2020 estimated that around 55% of the world's population currently lives in urban built spaces and it is predicted that this percentage will reach 70% by 2050 where 7 out of 10 people will be living in urban built spaces [16] with a decreased exposure to nature.

Here rises the research questions as to investigate whether this increase of urbanization and built spaces affect man's mental health? What qualities of architecture design nurture man's brain cognitively? Can physical qualities of space have an enriching and restoring impact on man's brains? How can these parameters be measured to have scientific-based outcomes?

A. *Neuro-Architecture and Mental Health*

Sustainable development goals believe that urban environments are becoming more significant health determinants. However, the research of how exact architectural design parameters change one's brain is still insufficient.

In 2003, neuroscientist Fred Gage coined the term 'Neuro-architecture', which is an interdisciplinary science that aims to understand the biological and sensory effect of built environments on one's brain [17] [18]. It aims to understand how the brain interacts with the surrounding environment over lifespan, develops biologically [19] [20] [21] then eventually changes emotions, behaviour and wellbeing [22] [23] [24]. With the increased urbanization, the goal of interdisciplinary studies like neuro-architecture and neuro-urbanism is to develop cross-sectional methods for optimizing how architecture affects one's brain.

This sheds the light on that the design decisions taken by architects affect how users perceive, feel, interact and evolve in the built space.

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Environmental psychology and behaviour research was based on self-reports, surveys, observations or post occupancy evaluation. Also, it used reports of changes in blood pressure, heart beats and facial expression to study 'how' users feel and react to environmental stimuli [25] [26] [27] and 'what' are the psychological responses. But neuro-architecture mainly investigates 'why' one responds this way and 'what' chemical changes happen in one's brain in response to spatial experience [28] [29] [30] to provide an evidence-based design approach.

Neuro-architecture research aims to create enriched environments that can enrich and nurture one's brain to enhance overall cognitive performance and mental well-being and reduce stress [31] [32] to be able to maintain strong brain resilience and cognitive reserve [20] [33] [4] [34]. This potential is supported by the concept of neuroplasticity [35] and neurogenesis [36].

One of the leading experts in this field of Neuro-architecture is Tye Farrow. His contributions have brought neuroscience into the stream of architectural discourse and he has shown how deliberate environmental design can have a profound effect on both physical and neurological health. The key design elements introduced by Farrow in his book, *Constructing Health* highlight the idea that architecture could actively promote human well-being [37], encompassing not just physical and sustainable health but also emotional and psychological well-being through:

- **Enriched Environments:** Farrow emphasizes the creation of environments that stimulate the brain and promote well-being. This includes incorporating elements like:

  1. **Nature:** Biophilic design principles to connect people with nature.
  2. **Variety:** Diverse spaces and experiences to stimulate the brain.
  3. **Vitality:** Dynamic and active environments that encourage movement and engagement.
  4. **Authenticity:** Genuine materials and spaces that resonate with people.
  5. **Optimism:** Uplifting and hopeful spaces that inspire positive emotions.
  6. **Sense of Occurrence:** engaging elements that create surprise and delight.
  7. **Legacy:** Spaces that contribute positively to future generations.

- **Salutogenic Design:** Based on Aaron Antonovsky's concept of salutogenesis, Farrow focuses on creating conditions that promote health rather than preventing illness. This involves designing spaces that:

  1. **Enhance sense of coherence:** People feel they can understand, manage, and find meaning in their environment.
  2. **Promote social connection:** Facilitate interaction and community building.
  3. **Support physical activity:** Encourage movement and exercise.
  4. **Reduce stress:** Create calm and restorative spaces.

B. *The Nurturing Nature*

Since the beginning of life, nature has always been an inspiration for built environment design as it is full of innovative structural and functional solutions. Now, with the growing interest in creating sustainable environments that prioritise long-term solutions and eco-friendly construction, nature is an important mentor through one's quest for creating sustainable built environments.

For years, environmental psychology and behaviour studies have always referred to nature as restorative environment. Studies found that continuous exposure to natural environments reduces stress [38], induces faster recovery from illness [39], and improves attention [40] [41] [42]. Inspired from nature, Frank Lloyd Wright developed the concept of 'organic architecture' that aims to create an environment that supports both human and ecological well-being [43]. Organic architecture developed through three main concepts:

- The original concept was to create harmony with nature and site, using natural materials, using natural light and air ventilation, and incorporating natural features like vegetation and water.

- The second concept developed as a style of architecture that uses natural forms, patterns and geometries, and incorporates natural organic shapes, patterns, and structures, as well as fluid curves and dynamic proportion and avoids hard lines to create harmony with the natural surroundings.

- The third concept developed to be a translation of models of living organisms using functional solution from nature to design as biomimicry to save energy and reduce environmental effect.

Sustainability writer Luana Ackaouy wrote that "The idea behind organic architecture is to put human life, nature and the built environment on the same level and build a sustainable ecosystem where all components support one another and thrive as a result". 'Biophilic design' also emerged that aims to integrate nature into design structures and environments to foster human interaction with the natural world and improve occupant productivity and well-being [27] [44] and inspired from the term biophilia which means 'love of nature' and stems from the idea that people are naturally connected to nature [25] [45] [46] [47] [48]. In COP21, biophilic design was discussed as an approach to fulfil the goals of green and sustainable architecture.

C. Neuro-psychology of Space Perception

To understand the psychology behind neuro-architecture, it is important to understand how one's brains perceive the surrounding space. Nobel Prize was awarded to John O'Keefe together with Edvard Moser and May Brit Moser in 2014 for their discovery of 'Place Cells' in the brain. In 1976, O'Keefe and his colleagues published an important study in Experimental Neurology. They discovered certain neurons in the hippocampus called Place Cells that are triggered when an animal navigates or is positioned in certain places in the environment. The discovery of 'place cells' and other spatial cell types related to it in the rodent brain helped in the discoveries the neural mechanisms of spatial information and spatial memory in humans [49] [50].

Other important types of spatial cells were discovered in the hippocampus such as place cells, grid cells, and boundary cells [51]. The boundary cells are neurons in the hippocampus that fires more when near an environmental boundary. Boundary cells activity suggests that the environmental geometry acts as an external sensory that impact cognitive mapping in the hippocampus [50].

The boundary neuron cells help to create a representational map of the shape of space around human beings [52]. Recent studies in both human and animal models suggest that spatial perception in the hippocampus system is boundary-based, rather than landmark-based [53]. This means that the neural system was found to be more sensitive to environmental boundaries and environmental geometries where spatial layout has a greater impact on the hippocampus rather than other aspects of visual scenes [54] [51].

Also, spatial configuration and layout, which is the arrangement and organization of spaces within a building or environment, have direct impact on the user's spatial experience. High integration and connectivity between spaces can enhance way finding, promote social interaction, and reduce violence [55]. Boundaries and form of space are main components that affect the architectural expression of space where:

1. 'Form' represents the physical property of the building such as geometry and structure that create the function of space within.

2. 'Boundaries' are the external outline that creates the physical form. They create the space within which activity takes place. The boundary represents division, separation, or limitations to space, it also creates the concepts of spatial perception. It gives space its physical limit and changes perception of space.

3. While 'space' is the open area, or volume, between structural elements, it is the negative area between positive solids. It is the volume where function takes place [56].

According to le Corbusier, 'Form Follows Function', but after the emergence of neuro-architecture, it becomes 'Form Follows Function, Emotions Follow Form'[57]. So, this research aims to investigate the impact of form of space boundaries on brain perception and brain chemicals testing abstract space boundaries like curved, circular and rectangular forms.

In aesthetic psychology especially in the first half of the 20th century, curves were perceived as quiet, merry, pleasant, weak, graceful and serene, while sharp angles are referred to as agitating, furious, robust, vigorous and hard [58] [59]. Curves are perceived as serene, graceful, tender and sentimental, while angles are perceived as robust, vigorous and agitating [59]. Aesthetic literature observed that rounded features and curved lines tend to be connected with pleasantness and contentment, whereas diagonal and angular arrangements tend to be associated with fear, curved lines are more ornamental and 'line of beauty' [60] inspired from natural analogies and patterns. Also, the preference of curves was investigated in different study areas such as in furniture [61], interior design [62] [23] [63] [64], product design [65] and car interiors [66].

With the evolution of neuroscience and over the past twenty years, the neurological impact of connection to nature and preference of curves became more interrelated [67] [68] [69] [70] [71].

An interesting a study using functional magnetic resonance imaging, demonstrated that the anterior cingulate cortex in the brain is activated when viewing objects with curvilinear contours and boundaries [72] [73]. This is the same part of the brain activated when viewing images of natural environments. The anterior cingulate cortex is a region involved in emotional regulation, emotion-based learning, memory and the reward pathway. The activation of anterior cingulate cortex leads to less stress and better emotional regulation and memory [63], [74].

On the other hand, another study using neuroimaging techniques demonstrated increased amygdala activation in response to the presentation of images of angular shaped objects [75]. Amygdala is also activated viewing images of urban views [72] [73]. This is an area in the brain responsible for behaviour, emotional regulation, learning, and very important in the automatic detection of danger. This suggests that the increase in urbanization associated with less natural environments can increase the activation of parts of brain that triggers the sense of danger and creates a continuous unconscious stressful fight or flight response. It also indicates that sharp-angled contours or boundaries induce the automatic 'fight or flight' response. This response over a long period of time can cause cognitive exhaustion and stress and impact negatively the overall mental health [28], according to the Cognitive Load Theory.

D. Existing Research and Gap in Neuro-architecture and Mental Health

The measuring techniques used in neuro-architecture is divided into stationary and mobile paradigms [21]. Stationary paradigm is held in controlled laboratory settings while participants view 2D images or 3D complex architectural settings, while measuring the brain instant activation using MEG, EEG or fMRI. This methodology measures the instant unconscious effect on the brain after a short-term exposure to a certain environmental stimuli over a few seconds [72] [76]. Functional magnetic resonance imaging and electroencephalography measure brain activity. In addition, neurophysiological effects are measured by monitoring electro dermal activity, or eye tracking, also, by measuring physiological parameters like blood pressure, heartbeat or skin conductance all after viewing real or virtual images of environmental and architectural settings for a short time interval in controlled laboratory conditions.

Another paradigm is the mobile techniques which allow physical interaction with the environment for a multi-sensory experience like virtual reality VR [77] [78] or CAVE [79] where participants wear portable brain-body imaging tool to measure the sensory experience of walking through the built environment [80] [23] [81] [21]. A study used the Emotiv EPOC, which is a low-cost EEG gadget, to investigate participants' response after moving for 25 minutes into a green space from urban setting in Edinburgh, Scotland. The results revealed positive emotions, such as lesser frustration, higher engagement, higher curiosity (arousal), and peacefulness [82].

All the current methods measure the physiological or neuro-psychological impact of special architecture setting, views, colours, textures or lighting on human users over a short-term period through a session in controlled conditions for minutes [77] [76] [72] [41] [83].

However, it is still challenging to measure the *long-term* effect of architectural stimuli or spatial experience on the brain and to investigate how a certain spatial experience can shape and mould the brain over time to enhance its cognitive performance for a sustainable mental health and well-being.

II. METHODOLOGY

As it is difficult to perform in-vivo studies on human brains after experiencing certain architectural setting over a long period of time, this research adopted a new methodology using comparative neuroscience, which is the study on animal models, to give tangible quantitative evidence of the impact of spatial experience on the brain cognitive performance and mental health.

This research is experimental research that adopts a comparative approach to measure the impact of form of space boundary; as the only variable; on spatial memory performance and oxidative stress defence mechanisms. It aims to test the hypothesis that different spatial experiences created by space boundaries can have a cognitive impact on the brain and hence change the overall brain performance and wellbeing. This hypothesis in investigated by both biological and behavioural testing techniques on animal models (mice) in controlled laboratory conditions where spatial experience in different space boundary formations is the only variable.

Comparative neuroscientific research uses mice as the genetic similarity between humans and mice reaches 85% where mice are like humans in terms of anatomy, physiology, and genetics. Among mammalian animals, mice are the most popular to use in comparative experiments in neuroscience due to their small size, low cost, short generation time and mature gene editing technology. Non-human animal studies are held under highly controlled conditions measuring one changed parameter at a time and can be applied repeatedly with different parameters [6]. Also, Brain imaging has been used in animal models to examine brain aging and to translate these findings [84]. In addition, an important benefit of using animal models is the ability to investigate biological parameters as cellular and molecular levels more easily than human examination to help in the definition and understanding the concept of cognitive reserve and brain maintenance and to provide scientific evidence not just a logical deductive evidence.

A large database of previous work also validates the use of mice as an animal model in environmental enrichment experiments as well as in cognitive, behavioural and neuroscientific experiments [36], [85], [86], [87], [88]. Environmental enrichment has proved its positive impact on cognitive reserve, cognitive performance and brain plasticity which is the ability of the nervous system to adapt anatomically and functionally to environmental stimuli [32] [31] [4] [5] and spatial experience [88]. Also, in studies on oxidative stress, environmental enrichment seemed to guard against oxidative stress by enhancing antioxidant defence mechanisms [89] [90].

Over the past 50 years, basic research using animals has helped to dramatically improve one's understanding of the brain and the nervous system. Nobel Prize was awarded in 2000 to Arvid Carlsson for the discovery of dopamine, a neurotransmitter that transmits signals in the brain and involves many diseases such as Parkinson's, using animals models including rats and mice. Also, in 2013, Nobel Prize was awarded for understanding proteins transportation in cells, using mice, rats and hamsters. Then in 2014, Nobel Prize was awarded to O'Keefe together with Edvard Moser and May Brit Moser for the discovery of Place cells responsible of positioning and navigation system in the brain, using rats [91].

The research hypothesizes that spatial experience of different formations of space boundaries can act as an environmental enrichment factor and that space perception changes the brain cognitive performance after long-term exposure. This is attained by measuring the impact of spatial experience on spatial memory by behavioural assessment using Y-maze brain and by biological measurements like acetylcholine responsible for memory, attention and learning, and finally, oxidative stress markers to evaluate which form had a positive and an enriching impact. The experiment was held at URAF-URESEARCH ANIMAL FACILITY under the supervision of qualified biologists and neuroscientists.

A. *Animal Model Sampling*

Twenty-four Mus Musculus male mice CD1 strain of ages from 8-10 weeks; which is equivalent to the age of adult human being; and of 25-32 grams weight are housed in three different spaces of the same material and space volume where spatial formations created by space boundaries is the only changing parameter.

According to a previous study by McQuail et al. (2021) [6], eight mice per group will be required to clarify whether there is a statistical difference

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between the experimental groups. Thus, in the present study, a total number of 24 mice (8 mice per group, three groups) is suitable for conducting the experiment.

Also, based on a previous study that concluded that three weeks is the minimum effective duration in longitudinal studies to measure changing parameters on mice in environmentally enriched studies [6], so in this study, animals are housed in the three spaces for four weeks duration.

B. *Space Design of Experimental Model*

Three different cages are designed and built with the same acrylic opaque material and the same space volume of a total of 1650 cm^2 where the area per animal is 276 cm^2 per animal.

- The first cage is a standard rectilinear cage of dimensions 47* 35* 21 that represents a large space with rectilinear edge walls as the control group Figures (1-a, b, and c).

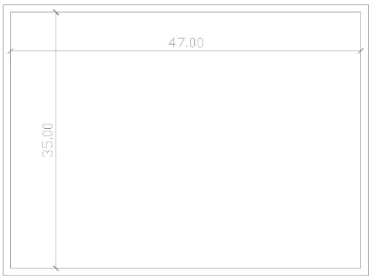

Fig. (1-a). Plan of open rectangular space

Fig. (1-b). Actual space upper view

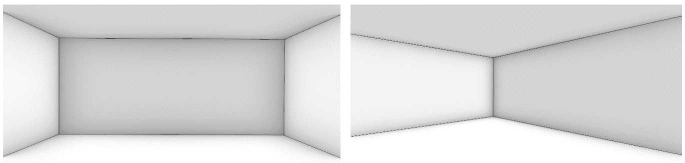

Fig. (1-c). Interior spatial experience of occupant's eye level (open rectangular)

The second cage has an outer circular boundary of 25 cm radius and an inner circle of 10cm radius and height of 21cm Figures (2-a, b, and c) that forms a narrow linear (corridor like) space with curved circular edge walls.

Fig. (2-a). Plan of narrow circular space

Fig. (2-b). Actual space upper view

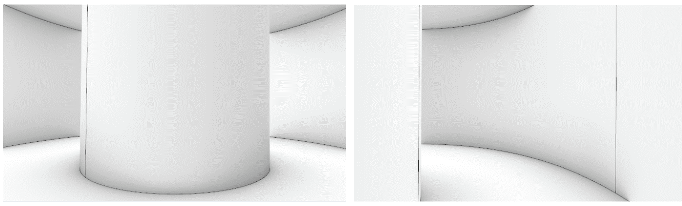

Fig. (1-c). Interior spatial experience of occupant's eye level (narrow circular)

The third cage has mixed formation of outer curvilinear boundaries and outer dimensions 54*40*21 cm and inner dimensions of 28*18*21 cm fig (1-c) that represents a narrow linear (corridor like) space with a mix of curved and rectilinear edge walls as in Figures (3-a, b, and c).

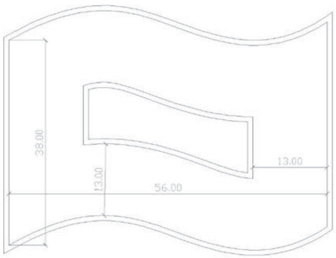

Fig. (3-a). Plan of narrow mixed rectilinear/curvilinear space

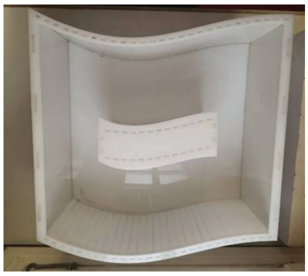

Fig. (3-b). Actual space upper view

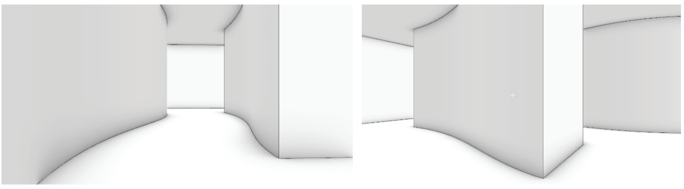

Fig. (3-c). Interior spatial experience of occupant's eye level (narrow mixed rectilinear/curvilinear space)

1. Phases of Experiment Procedures

The experiment procedures consisted of three different phases:

a. *Body weight monitoring*

During the housing period the mice body weight is measured every week for four weeks to monitor the mice general health.

b. *Behavioural test*

After four weeks the mice are subjected to Y-Maze test [92]. Y-Maze Test is a test used to assess short-term spatial recognition memory and is based on the innate desire of rats to investigate new environments. It is previously used to study the effects of age, environmental enrichment, the use of different medications and dietary supplements, as well as different stressors, on spatial memory skills [3].

A study held in 2021 comparing the results of animal spatial performance in Y-maze to human experience concluded that Y-maze is a sensitive test that can be used to evaluate working memory and cognitive flexibility in a variety of species, including humans. It is an extremely useful behavioural test that is easy to use and broadly applicable with 'exceptional translational relevance' as mentioned in the study [93].

The Y-maze is made up of three identical arms mounted in the shape of a "Y." Each arm is typically 37 cm long and 8.75 cm wide with walls made of opaque material as in Fig. 2. During the experiment, which usually lasts 5 to 8 minutes, allows the animals to freely explore the maze.

The order in which the arms are entered is noted, and the proportion of spontaneous alternation; which is the quick successive entry of three arms; is used to assess the animals' working memory capacity [94].

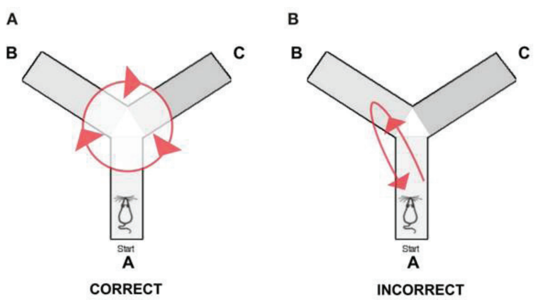

Fig. 4. Showing the Y-Maze test with illustration to correct and incorrect alternations [3]

c. *Biological markers*

The animals are sacrificed to collect brain tissue and measure the percentage of a chemical called acetylcholine esterase 'AChE' and oxidative stress markers SOD, GSH, CAT and MDA according to the experiment methods mentioned in [95].

1. Acetylcholine esterase

Acetylcholine esterase AChE is a key enzyme in the nervous system found between the nerve cell and the muscle cell. It breaks down the neurotransmitter acetylcholine 'ACh' [96]. Acetylcholine 'ACh' is an important neurotransmitter responsible of memory, attention and learning in the brain. High levels of AChE and Low levels of Ach are associated with Alzheimer's disease and other neurodegenerative disorders [86]. That is why medications of Alzheimer's disease, acetylcholine esterase AChE activity as high levels of AChE inhibitors.

2. Oxidative stress markers

Environmental enrichment can have a positive impact on oxidative stress defence mechanisms [97]. Oxidative stress, it is defined as the generation of an imbalance between the production and storage of reactive oxygen species (ROS) in cells and tissues of the brain and the ability of the body to detoxify itself [98].

Oxidative stress causes impairment of emotional and mental well-being. It has negative impact on normal central nervous system CNS and can cause damage to the brain. It is involved in many neurodegenerative disorders such as Alzheimer disease, Huntington disease, and Parkinson disease, as well as other neuropsychiatric disorders such as anxiety disorders and depression [2] [89] [99].

Formation of free radicals ROS is induced by both internal and external factors [100]. Internal factors as immune cell activation, inflammation, infection, cancer, excessive exercise, mental stress, and aging. External factors as exposure to environmental pollutants, heavy metals, certain drugs chemical solvents, cigarette smoke, alcohol, and radiations [101].

Studies in aging humans and animals showed that environmental cognitive stimulation known as environmental enrichment affected behavioural symptoms in mice with Alzheimer-like disease [102]. Another study monitored a positive impact of environmental enrichment change in the Alzheimer's oxidative damage in the brain of mice

[89]. Also, another study showed that compared to control animals, rats exposed to environmental enrichment had greater antioxidant levels and reduced oxidative stress markers [97]. Cells induce an antioxidant defensive system such as superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) to fight free radicals and to protect themselves from ROS-induced cellular damage [103].

d. Results

Both behavioural and biological tests are conducted, and results are analysed statistically using The ANOVA & Duncan's to measure the impact of spatial experience created by form of space boundaries on spatial memory and brain performance after long term exposure to certain spatial experiences.

ANOVA test is used to analyse three different treatments (exposure to either open rectilinear space, narrow circular space, or mixed rectilinear/ curvilinear space) i.e. one factor with three levels [104]. ANOVA conditions have been met in the present data which are:

1) Normality assumption, according to the Shapiro test.
2) Homogeneity of variance.
3) Observations are independent of each other (different groups).

Regarding the sample size, calculations were executed using GPower software version 3.1.9.4.

1. Body weight results

In graphical representations, the spaces will be referred to as following:

Space (1) open rectangular space as NORMAL
Space (2) narrow circular space as CIRCULAR
Space (3) narrow mixed rectilinear-curvilinear space as CURVILINEAR or WAVY

TABLE I
BODY WEIGHT CHANGES IN THE MICE HOUSED IN THE OPEN RECTILINEAR SPACE, CIRCULAR NARROW SPACE AND MIXED CURVILINEAR NARROW SPACE. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Time (week)	Open Rectilinear space (1)	Circular narrow space (2)	Mixed Curvilinear/ rectilinear narrow space (3)	Effect of cage shape
0	31.88 ± 1.84^{A}	33.38 ± 1.73^{A}	31.13 ± 0.97^{A}	$F_{2,21}$=0.538, P=0.592
1	33.50 ± 1.89^{A}	34.25 ± 1.78^{A}	35.00 ± 1.89^{B}	$F_{2,21}$=0.164, P=0.850
2	35.50 ± 1.54^{A}	36.00 ± 1.74^{A}	35.50 ± 0.96^{B}	$F_{2,21}$=0.040, P=0.961
3	35.38 ± 1.03^{A}	37.25 ± 1.70^{A}	36.00 ± 0.98^{B}	$F_{2,21}$=0.556, P=0.582
Effect of time	$F_{3,28}$=1.14, P=0.349	$F_{3,28}$=1.14, P=0.407	$F_{3,28}$=1.14, P=0.043	

In each row *, #: represents significant differences (P<0.05), as compared to the mice housed in the rectilinear open space, circular narrow space and mixed curvilinear/rectilinear space, respectively. In each group, among the various time intervals, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

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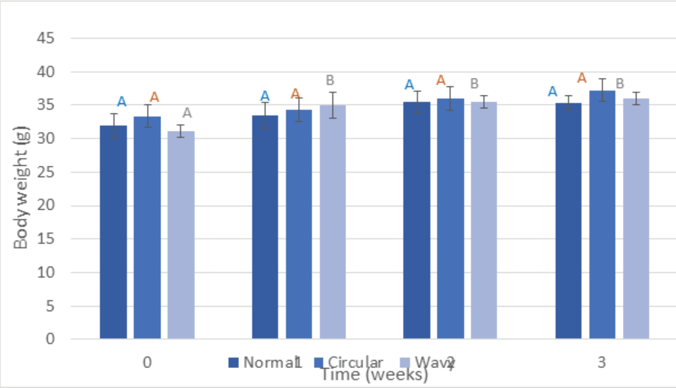

Fig. 5. Body weight changes in the mice housed in the open rectilinear space (normal), circular narrow space (circular) and mixed curvilinear/rectilinear spaces (wavy)

2. Behavioural test results

After measuring percent of correct alternations in three spaces as in Table II, the results showed a significant increase in the percentage of alternations of mice in the Y-Maze housed in the third space of mixed curvilinear-rectilinear formation for four consecutive weeks than the alternations of mice housed in the open rectilinear and narrow circular spaces. This suggests that mice had intact working memory and better prefrontal cortical performance.

Also, results indicate a significant decrease in the percentage of alternations in narrow circular space than both the control group in open rectilinear space and the mixed rectilinear/curvilinear space as in Fig. 4. The results suggest that merging both rectilinear and curvilinear geometries created a spatial experience that gave the mice a better spatial reference memory and a healthy hippocampus as poor abilities in alternations in maze test and spatial memory tasks indicate poor performance of the hippocampus in the brain [50]. This can be caused by defects in the neural system and spatial cells controlling the spatial cognition of the surrounding.

TABLE II
RESULTS SHOWING PERCENTAGE OF CORRECT ALTERNATIONS IN THREE SPACES.

Cage shape	% Alternation
Open Rectilinear (1)	20.14 ± 0.07^{B}
Narrow Circular (2)	18.38 ± 0.22^{A}
Narrow mixed rectilinear/ Curvilinear (3)	23.31 ± 0.72^{C}
	$F_{2,21}$=32.70, P=0.000

The results of Y-maze parameters in the mice housed in spaces with open rectilinear space, narrow circular and narrow mixed rectilinear/ curvilinear boundaries are presented in Fig. 6. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

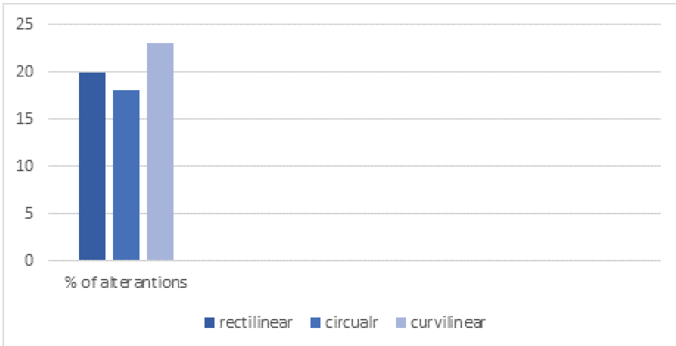

Fig. 6. Bar chart showing the percentage of alternations in three space design (open rectilinear-narrow circular- mixed rectilinear/curvilinear)

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3. Biological markers results

After four weeks and after conducting the behavioural tests, animals hare sacrificed, results of both acetylcholine levels and oxidative stress markers are analysed statistically using The ANOVA & Duncan's as in Table III.

TABLE III
ALL BIOLOGICAL MARKERS RESULTS IN THE BRAIN OF MICE HOUSED IN THE OPEN RECTILINEAR, NARROW CIRCULAR AND MIXED RECTILINEAR/CURVILINEAR SPACE FORMATIONS. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Cage shape	MDA (nM/g tissue)	GSH (nM/g tissue)	CAT (U/g tissue)	SOD (U/g tissue)	ACHE (U/g tissue)
Open rectilinear (1)	1.02 ± 0.05^{B}	2.49 ± 0.28^{B}	2.07 ± 0.14^{B}	87.43 ± 4.38^{A}	0.14 ± 0.004^{B}
Narrow Circular (2)	2.58 ± 0.16^{C}	0.22 ± 0.01^{A}	1.02 ± 0.08^{A}	83.01 ± 3.26^{A}	0.19 ± 0.01^{C}
Narrow mixed rectilinear/ Curvilinear (3)	0.39 ± 0.05^{A}	4.69 ± 0.25^{C}	3.85 ± 0.52^{C}	83.76 ± 2.12^{A}	0.11 ± 0.01^{A}
	$F_{2,21}$=119.2, P=0.000	$F_{2,21}$=103.4, P=0.000	$F_{2,21}$=308.7, P=0.000	$F_{2,21}$=0.491, P=0.619	$F_{2,21}$=17.71, P=0.000

a. Acetylcholine esterase levels

Results of acetylcholine levels collected as in Table IV indicate a significant increase in acetylcholine esterase concentration in brain tissue of mice housed in narrow circular spaces which indicate lower levels of acetylcholine which means less attention, memory and learning abilities. Results also indicate significant decrease of acetylcholine estarese in curvilinear spaces which indicates a better level of acetylcholine ACh as presented in Fig. 5.

TABLE IV
THE LEVELS OF ACETYLCHOLINE ESTERAE (AChE) IN THE BRAIN OF MICE HOUSED IN THE OPEN RECTILINEAR, NARROW CIRCULAR AND MIXED RECTILINEAR/ CURVILINEAR SPACES. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Cage shape	ACHE (U/g tissue)
Open rectilinear (1)	0.14 ± 0.004^{B}
Narrow Circular (2)	0.19 ± 0.01^{C}
Narrow mixed rectilinear/ Curvilinear (3)	0.11 ± 0.01^{A}
	$F_{2,21}$=17.71, P=0.000

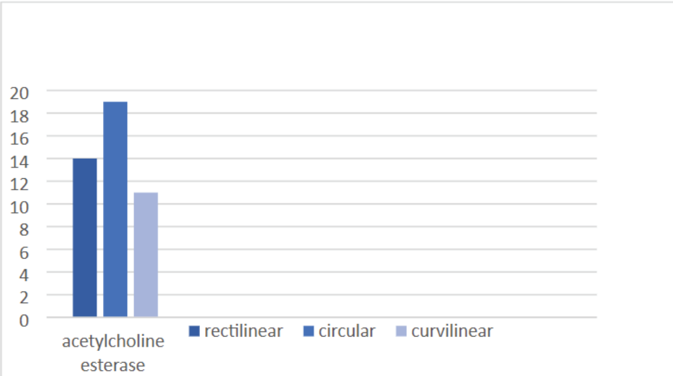

Fig. 7. The levels acetylcholine esterase (AChE) in the brain of mice housed in the open rectilinear normal, narrow circular and mixed rectilinear/curvilinear spaces. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

4. Oxidative stress markers

Anti-Oxidants as SOD, GSH and CAT that control the formation of free radicals to maintain a healthy brain and body. Also, another marker of the presence of oxidative stress is MDA.

a. Glutathione (GSH) levels:

Glutathione is an important antioxidant that protects against oxidative stress. It plays an important role in the central nervous system as a neurotransmitter and neuromodulator. Glutathione is also necessary for increasing the effectiveness of neurotransmitters such as dopamine, serotonin, and glutamate [105], all of which play important roles in mood regulation.

Results in Table V show significant decrease of GSH in narrow *circular* space (higher level of oxidative stress) and significant increase of GSH in mixed rectilinear/*curvilinear* space formation (lower level of oxidative stress).

TABLE V
THE LEVELS OF GLUTATHIONE (GSH) IN THE BRAIN OF MICE HOUSED IN THE OPEN RECTILINEAR, NARROW CIRCULAR AND MIXED RECTILINEAR/CURVILINEAR SPACES. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Cage shape	GSH (nM/g tissue)
open Rectilinear (1)	2.49 ± 0.28^B
Narrow Circular (2)	0.22 ± 0.01^A
Narrow mixed rectilinear/ Curvilinear (3)	4.69 ± 0.25^C
	$F_{2,21}$=103.4, P=0.000

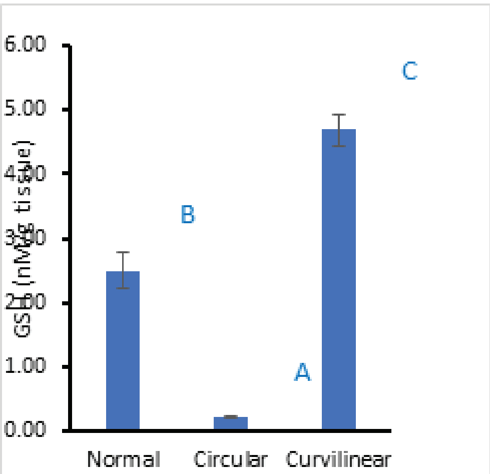

Fig. 8. The levels of glutathione (GSH) in the brain of mice housed in the open rectilinear, narrow circular and mixed rectilinear/curvilinear spaces. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

b. Superoxide dismutase (SOD):
Superoxide dismutase (SODs) is a very important antioxidant that acts as a frontier against oxidative stress in the body [106]. Results show insignificant change between three spaces as in Table VI.

TABLE VI
THE LEVELS OF SUPEROXIDE DISMUTASE (SODs) IN THE BRAIN OF MICE HOUSED IN THREE SPACES. DATA ARE PRESENTED AS MEAN± STANDARD ERROR OF MEAN.

Cage shape	SOD (U/g tissue)
Open Rectilinear (1)	87.43 ± 4.38^A
Narrow Circular (2)	83.01 ± 3.26^A
Mixed rectilinear/ Curvilinear (3)	83.76 ± 2.12^A
	$F_{2,21}$=0.491, P=0.619

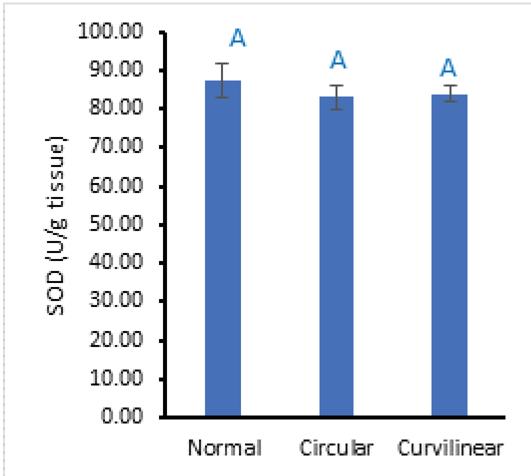

Fig. 9. The levels of Superoxide dismutase (SODs) in the brain of mice housed in three spaces. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

c. Catalase (CAT):
Catalase is one of the important antioxidants produced by the body. Its deficiency or malfunctioning is associated with many age-related diseases likee Alzheimer's disease, Parkinson's disease, bipolar disorder, cancer, and schizophrenia [107].

Results show significant decrease of CAT in narrow *circular* space (higher level of oxidative stress) and significant increase of CAT in mixed rectilinear/ *curvilinear* space (lower level of oxidative stress) as in Table 7.

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TABLE VII
THE LEVELS OF CATALASE CAT IN THE BRAIN OF MICE HOUSED IN THE OPEN RECTILINEAR, NARROW CIRCULAR AND NARROW MIXED RECTILINEAR/CURVILINEAR SPACES. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Cage shape	CAT (U/g tissue)
Open Rectilinear (1)	1.02 ± 0.08^{A}
Narrow Circular (2)	33.85 ± 1.83^{B}
Narrow mixed rectilinear/ Curvilinear (3)	2.07 ± 0.14^{A}
	$F_{2,21}=308.7$, P=0.000

TABLE VIII
THE LEVELS OF MALONDIALDEHYDE (MDA) IN THE BRAIN OF MICE HOUSED IN THE OPEN RECTILINEAR< NARROW CIRCULAR AND MIXED RECTILINEAR/CURVILINEAR SPACES. DATA ARE PRESENTED AS MEAN ± STANDARD ERROR OF MEAN.

Cage shape	MDA (nM/g tissue)
Open Rectilinear (1)	1.02 ± 0.05^{B}
Narrow Circular (2)	2.58 ± 0.16^{C}
Narrow mixed rectilinear/ Curvilinear (3)	0.39 ± 0.05^{A}
	$F_{2,21}=119.2$, P=0.000

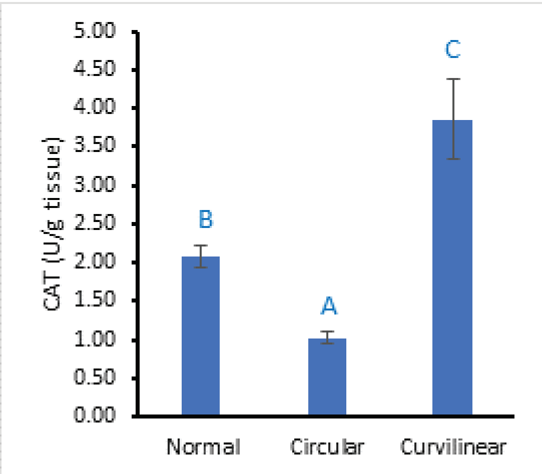

Fig.10. The levels of Catalase CAT in the brain of mice housed in the open rectilinear, narrow circular and mixed rectilinear/ curvilinear spaces. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

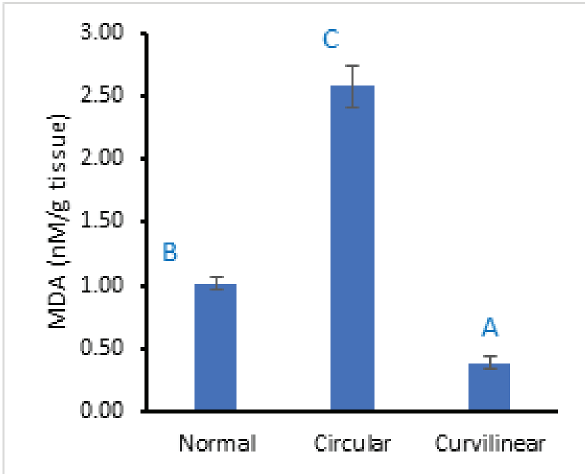

Fig. 11. The levels of malondialdehyde (MDA) in the brain of mice housed in the open rectilinear, narrow circular and mixed rectilinear/curvilinear spaces. Data are presented as mean ± standard error of mean. Among the different cage shapes, the means marked with similar superscript letters are insignificantly different (P>0.05), whereas those different ones are significantly different (P<0.05).

d. Malondialdehyde (MDA)

Malondialdehyde (MDA) is used as a marker of the development of oxidative stress (Keller et al., 2005; Maulik & Das, 2000). Its decrease is beneficial to body cells. Results in Table VIII show significant increase of MDA in narrow circular space (higher level of oxidative stress) and significant decrease of MDA in mixed rectilinear/curvilinear space formation (lower level of oxidative stress).

III. DISCUSSION

The research behavioural and biological results offer a scientific-based evidence of the impact of a certain architectural quality; like form of space boundaries; over long period of time, on brain perception, altering chemicals in the brain and hence its overall performance and wellbeing.

The available scientific literature discussing the preference of curves used different synonyms of curves like (curvilinear- organic- rounded- smooth- and circular), but this research sheds the light that pure circular geometries can have a completely different impact on our brains than the curvilinear forms. They are not the same and impact the brain differently.

The results showed that animal models (mice) housed in spaces with mixed formations of rectilinear/curvilinear boundaries had a higher percentage of alternations in the Y-maze behaviour test. Higher percentage of alternations is an indicator of better spatial working memory, better cognitive performance and healthier hippocampus [92] [93].

Regarding body weight change, it is normally expected that mice body weight will increase gradually throughout the experimental duration. However, in group housed in mixed rectilinear/ curvilinear space, body weight change was slightly pronounced ($p=0.043$). This finding may be linked to the reduced oxidative stress as confirmed by the reduced lipid peroxidation and increased antioxidant activity and subsequent increased feed intake. It is documented that a high feeding rate is largely associated with improved mood and reduced stress [108].

Also, mixed rectilinear/curvilinear space form had a restorative effect on brain chemicals responsible for memory, attention and learning. Experiencing this space, increased the percentage of glutathione GSH and catalase CAT, which are very important antioxidants in the brain. They help in regulating neurological functions especially assigned with learning, memory, and neuroplasticity [109]. As a result, glutathione protects these neurotransmitters from damage and degradation, preserving and increasing their efficacy and lowering the risk of neurodegenerative disorders. Anti-oxidants act as a frontier against many psychological and neurological diseases and help to maintain brain health and mental wellbeing.

On the other hand, the narrow circular space did not have the same impact. Pure circular geometries had stressful impact even more than pure rectangular forms or mixed formations. Experiencing circular spaces reduced spatial memory performance, increased levels of acetylcholine esterase AChE that inhibits acetylcholine ACh responsible for memory and attention. Also, circular spaces reduced levels of ant-oxidants like GSH and CAT. This may be related to the cognitive load theory that certain geometries like curves and organic forms inspired from nature are perceived automatically without stressing the brain, while sharp angled rectangular forms, and here in this study, pure circular forms, can trigger the fight or flight response and cause brain stress over time.

This promotes that incorporating curvilinear formations in architectural design along with rectilinear geometries can have not only a psychological effect but also a neurological restorative impact on one's brain and overtime can enhance the overall cognitive performance and mental wellbeing for sustainable healthy minds.

IV. CONCLUSION

The practical implications of this research are that it blurs the line between architecture and science and paves the road for architects to have quantitative measurable impact of their designs on users. For future research, it can be used as a tool to measure the long-term effect of other physical architectural elements like colours, materials and lighting. It can be investigated one parameter at a time or combined, which can be translated to human experience for a complete scientific guideline for architects.

One of the main limitations of the research is the novelty of this approach in architecture so designing the methodology was challenging. In addition, as architecture is a multi-sensory experience, it is difficult to investigate one parameter at a time. Also, the presence of user's personal variance, gender, cultural background and personal experiences can change their perception of space, which makes it difficult to sum the architectural perception in an element or two. However, this methodology can be used as a tool to investigate how certain architectural elements can alter the brain and change its functions on the long term especially that the comparative approach of using animal models is applicable in research in cognitive neuroscience, environmental enrichment and cognitive psychology.

Actually, architects can benefit from new knowledge of neuroscience as it can help to study how the design of classrooms can support the cognitive activities and learning abilities of students, how the design of offices and laboratories can enhance creativity and productivity, and how the design of healthcare facilities can promote recovery and wellbeing. This is a first step towards a regenerative architecture that is based on neuro-biological principles for overall mental wellbeing to build a strong cognitive reserve and resilience as a frontier against neuro-degenerative disorders for sustainable healthy minds as sustainable development needs healthy brains.

This research sheds light on the multidisciplinary approach of architecture and urban design. The science-based method adopted clarifies that architects and urban designers can seek evidence using scientific tools and including scientific approaches in design decisions. Creating inspiring spaces which affect the users' moods, health and well-being can be easily verified using experimentation. Thus, sustainable design is not limited to applying surficial strategies, but also can be included into actual evaluation based on biological variations.

Thus, sustainable architecture and wellbeing can be proven scientifically to inform architects and designers regarding a revolutionary approach in designing spaces.

DECLARATIONS

List of Abbreviations

SDG's: Sustainable Development Goals
WHO: World Health rganisation
DALY's: Disability adjusted life years
SRT: Stress reduction theory
ART: Attention restoration theory
CLT: Cognitive load theory
MEG: Magnetoencephalography
EEG: Electroencephalography
fMRI: Functional magnetic resonance imaging
VR: Virtual reality
AChE: Acetylcholine esterase
ACh: Acetylcholine
SOD: Superoxide dismutase
GSH: Glutathione
CAT: Catalase
MDA: Malondialdehyde
CNS: Central nervous system
ROS: Reactive oxygen species

Ethics approval and consent to participate

The Institutional Animal Care and Use Committee approved the experimental procedures (approval no. URAF- F1423). All animal housing and experiments were conducted in strict accordance with the institutional Guidelines for Care and Use of Laboratory Animals.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author upon request.

Competing interests

The authors have declared no conflict of interests.

Funding

No funding was received for conducting this study.

Authors' contribution

The authors confirm contribution to the paper as follows: Study conception and design: Elghor A., Shafik Z., Ali A., Elhusseiny M.; data collection: Elghor A., Ali A., Elhusseiny M.; Analysis and interpretation of results: Elghor A., Ali A.; Draft manuscript preparation: Elghor A., Shafik Z., Elhusseiny M. All authors reviewed the results and approved the final version of the manuscript.

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