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## Application of AR and 3D technology for learning neuroanatomy

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## Abstract

Neuroanatomy is a notoriously challenging subject for many students to master. The phenomenon of students having difficulties in mastering this discipline is so widespread that Ralph F.

Jozephivicz coined term "neurophobia" in 1994, which he defined as "*a fear of neural sciences and clinical neurology that is due to the students' inability to apply their knowledge of basic sciences to clinical situations*".

In order to successfully learn neuroanatomy, student must possess strong spatial skills in order to be able to visualise complex neuroanatomical structures and their relations to each other. Traditional learning resources such as textbooks and atlases can only provide 2D rendering of the complex 3D neuroanatomical structures, which makes learning process very cumbersome.

Cadaveric dissection, which is currently regarded a golden standard of learning and teaching anatomy, present some major challenges, from both practical and ethical angles, which need to be taken into consideration.

With an increasing demand for neurologists and specialists in adjacent disciplines, neurophobia amongst medical and life-science students presents a serious issue.

Using emerging technologies such as 3D and augmented reality (AR) for teaching anatomy (including neuroanatomy) has been proven to be effective in improving academic performance of the students. These technologies add elements of novelty, which helps make the learning experience more exciting and enjoyable for students. This, in turn, increases students' motivation and, subsequently, improves their learning outcomes.

After looking at the previous research, the decision was made to develop a mobile application, featuring AR element and an interactive 3D model, which could be used as a learning tool by

anyone who wishes to learn brain anatomy. The app features three scenes (AR, 3D, and 2D, and a

short quiz. AR functionality relies on an accompanying PDF booklet, which contains AR-targets and instructions on how to download and use the app.

The app was tested by twelve volunteers that were recruited through the XRDRN network (<u>www.xrdrn.org/</u>) and social media (e.g. linkedin.com, twitter.com). Overall, findings indicate the high usability of the application. The study results also demonstrated significant improvement of the neuroanatomy knowledge among the participants.

While this study has some limitations, the developed application has the potential to become a valuable learning aid for anyone seeking to learn neuroanatomy.

### Keywords

Neuroanatomy, neurophobia, augmented reality, 3D, brain anatomy, independent learning

## **1.1 Introduction**

Anatomy tends to be a very challenging subject for students to study, and neuroanatomy even more so (Javaid *et al.*, 2018). The difficulty lies not only in having to learn and memorise large amounts of information, and to study highly complex neuroanatomical structures, but also in understanding the spatial relationships and interactions between them. Textbooks and anatomical atlases are currently the main resources for teaching and learning anatomy (Peterson and Mlynarczyk, 2016). While traditional resources certainly have their place in anatomy education, students require other studying materials to learn the subject more in depth. Historically, cadaveric dissection has been considered a gold standard of anatomy education and it remains as such to this day. However, using cadavers as a teaching resource comes with a number of significant ethical and practical challenges, which cannot be ignored (Darras *et al.*, 2019). Finally, the ongoing Covid-19 pandemic presented students and lecturers alike with the new issues, such as limited access to dissection labs and face-to-face teaching.

A number of researchers are suggesting that a new approach to teaching and learning neuroanatomy would be beneficial to students (McLachlan *et al.*, 2004; Moro *et al.*, 2017; Henssen *et al.*, 2020; Sotgiu *et al.*, 2020). Traditional methods, such as textbooks and anatomical atlases are not sufficient due to their two-dimensional nature and must be complimented by the additional materials (Kockro *et al.*, 2015; Stepan *et al.*, 2017). Realistic 3D models with which users can interact would help to flatten the steep learning curve in neuroanatomy education focusing on the brain (Biassuto, Caussa and Criado del Río, 2006; Bogomolova *et al.*, 2020; Mendez-Lopez *et al.*, 2021). It could also offer

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a good alternative to the existing challenges of managing cadaveric dissections for many higher education institutions worldwide.

Mobile devices such as smartphones and tablets are quite ubiquitous, and the vast majority of the UK population already own at least one device (Kipper, 2013). Embracing this technology and using it to facilitate learning process seems like an obvious step forward. Augmented Reality (AR) can be used to develop a new, more engaging way to learn and teach anatomy using mobile devices (Weeks and Amiel, 2019). Moreover, it gives users an opportunity to employ a more active learning style by actively engaging with the 3D digital models overlaid onto the real world instead of passively consuming content by reading a textbook or by watching educational videos (Kugelmann *et al.*, 2018).

New technologies such as AR apps featuring interactive 3D models have the potential to make learning process more enjoyable and appealing for students and could potentially reduce the time required to gain and to consolidate knowledge (Weeks and Amiel, 2019). This is especially relevant for medical students and trainees, as medical knowledge is rapidly expanding (Alfalah *et al.*, 2019). Alternative ways of learning anatomy are thus needed.

The aim of this research was to develop an interactive application for mobile devices that can be used to acquire and consolidate knowledge of the complex physiological and spatial relationships amongst the major structures of the brain. This was achieved through the completion of the following objectives:

- 1. Building a body of knowledge about digitally augmented neuroanatomy education, its effectiveness in contrast to the traditional teaching methods was built.
- Building upon an anonymised medical MRI dataset to create an anatomically accurate 3D model of the brain.
- 3. Developing an educational mobile app to allow the user to learn and review the brain anatomy, consolidating their knowledge through self-paced testing in a number of ways:
  - a) by viewing augmented anatomical models
  - b) by interacting 3D models of the brain

c) by viewing the neuroanatomical structures on the labelled MRI scans and 2D illustrations

- 4. Conducting user-testing looking at knowledge development and usability
- 5. Critically reflecting on experimental and design outcomes

### **1.2 Theoretical Background**

3D and AR-based applications can valuable learning aids, helping students visualise complex 3dimensional neuroanatomical structures and develop their spatial skills which are crucial for successfully mastering neuroanatomy.

### **1.2.1 Changing Curricula and Emerging Challenges**

Upcoming advances in biological sciences and medicine result in increasing complexity and raising volume of content of medical and life science education, however the time available for students remains extremely limited (Ruthberg *et al.*, 2020). Despite the rapid development of medical sciences, students are still being taught using very conservative and old-fashioned methods (Alfalah *et al.*, 2019). Accommodating constantly changing and expanding curricula using both traditional and novel methods is an enormous challenge that medical schools and universities are currently facing (Alfalah *et al.*, 2019).

Currently anatomy is commonly taught in the early stages of the undergraduate programmes. Any further progress, not to mention a successful career in the medical and surgical fields is not possible without it (Alfalah *et al.*, 2019; Washmuth *et al.*, 2020). However, the latest developments in medical science are making it necessary for many universities to implement changes in their curricula, which often result in reduction of hours dedicated to teaching anatomy (Azer and Eizenberg, 2007; Ruthberg *et al.*, 2020). There is an ongoing shift towards students' self-directed learning as face-to-face teaching time is reduced (Moro *et al.*, 2017). All these tendencies resulted in decreasing numbers of skilled anatomists available and anatomy becoming a disappearing discipline (Papa and Vaccarezza, 2013). Since anatomy is one of the key areas of knowledge for medical professionals, this is highly problematic and medical students and lecturers alike have expressed their concerns on repeated occasions (Papa and Vaccarezza, 2013; Berrios Barillas, 2019; Ruthberg *et al.*, 2020).

### **1.2.2** Cadaveric Dissection as a Teaching Method

Cadaveric dissections and prosections are currently regarded as the most effective methods for teaching anatomy to students (Biassuto, Caussa and Criado del Río, 2006; Ghosh, 2017; Ruthberg *et al.*, 2020; Washmuth *et al.*, 2020). However, cadaveric dissection as a teaching method comes with many significant challenges, which are difficult to ignore. Emotional distress and anxiety,

which can range from mild to acute, experienced by students, are among these challenges (Allison *et al.*, 2021; Zubair, Waheed and Shuja, 2021). Some students might adopt a "detachment" defence mechanism and stop regarding cadaver as a human being (Zubair, Waheed and Shuja, 2021). Health and safety issues, together with high costs associated with embalming, storage and other practicalities should also be taken into consideration. For example, exposure to formaldehyde and other potentially harmful chemicals that are commonly used in the embalming process can present a serious risk to the health and safety of students and university staff (McLachlan and Patten, 2006; Washmuth *et al.*, 2020).

Moreover, there are a lot of legal regulations that must be observed, as stated in Human Tissues Act and the Anatomy Act (Papa and Vaccarezza, 2013). In the UK these regulations are stated in the Anatomy Act 1984 and in the Human Tissue Act 2006 (the latter only applies to Scotland). There are also some serious ethical and moral aspects associated with cadaveric dissection. Public perception of practice of cadaveric dissection is changing, especially after events such as the scandal involving Alder Hey Hospital and Prof Dick van Velzen (https://www.theguardian.com/uk/2005/jun/21/alderhey.helencarter), as well as controversial Body Worlds Exhibition by Gunther von Hagen (McLachlan and Patten, 2006).

Finally, some crucial aspects of live human anatomy, such as lifelike organs and tissues, and physiological processes such as bleeding or pulsating, are missing in a cadaver. McLachlan and Patten (2006) point out that some students even feel that cadavers are clinically irrelevant due to their organs' colour, texture, smell, and immobility.

### 1.2.3 Neuroanatomy and Neurophobia

Neuroanatomy is a section of anatomy that many students find excessively complex and confusing, and, as a result, feel anxious about studying it and as a result are unwilling to choose a career that would require thorough knowledge of neuroanatomy (Edwards-Bailey *et al.*, 2021). Neurological and neurosurgical conditions are quite common and, to ensure that patients have access to proper care, general practitioners must have sufficient knowledge of neuroanatomy and be aware of the pathological processes that can affect nervous system, so they can make an appropriate referral, point out Edwards-Bailey *et al.* (2021). Thorough knowledge of neuroanatomy is crucial for neurosurgeons, as this speciality is the most liable to malpractice: around 19.1% of neurosurgeons facing a claim a year (Cobb *et al.*, 2016). It is clear that neurophobia constitutes a serious problem as a large number of patients with neurological conditions, as well as the ageing population mean increased demand for neurologists (Sotgiu *et al.*, 2020).

In order to successfully learn neuroanatomy, students must possess good spatial mapping skills, however, it is not a requirement for the candidates enrolling in medical schools, nor the medical

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schools' curricula focus on developing such skills (Ridsdale, Massey and Clark, 2007; Mendez-Lopez *et al.*, 2021). Javaid et al. (2018) suggest that purposefully designed Computer Assisted Learning resources can help to alleviate neurophobia in students. AR-based applications can help anatomy (and especially neuroanatomy) students to acquire better understanding of spatial relationships between different neuroanatomical structures (Chien, Chen and Jeng, 2010; Mendez-Lopez *et al.*, 2021). Besides, the use of AR-based applications can help students work on improving their spatial abilities, even if they had relatively poor orientation skills prior to their experience with AR (Wu *et al.*, 2013; Bogomolova *et al.*, 2020; Mendez-Lopez *et al.*, 2021).

In-depth knowledge of neuroanatomy is more important than ever with the rising popularity of minimally invasive neurosurgery (keyhole surgery). This type of surgery offer a better chance of successful outcome by allowing to minimise damage to the surrounding tissues. On the other hand, there are also significant risks associated with the keyhole surgery, as the surgeon cannot clearly see what she or he is doing, so even though minimally invasive neurosurgical procedures are becoming increasingly common, they are still challenging to learn and perform safely (Bernardo, 2017). There is evidence demonstrating that ability to visualise and interact with neuroanatomical structures in 3D improves neurosurgeons' confidence and performance (Bernardo, 2017; Mendez-Lopez *et al.*, 2021). It is also known that learning in 2D is much more taxing for neurosurgeons' cognitive abilities and leads to longer operation times, as well as increasing the chance of error (Bernardo, 2017). Neuroanatomy currently is mostly learned using traditional resources such textbooks, 2D imagery, or post-mortem specimens. However, none of these resources can provide an accurate representation of variations of human neuroanatomy (Panesar *et al.*, 2019).

As mentioned above, cadaveric specimens, while being highly effective and valuable resources to support anatomy education, have serious limitations when it comes to teaching about the nervous system (Papa and Vaccarezza, 2013). Written resources are usually densely packed with information, most of which is not required for the undergraduate level. 2D resources such as illustrations, photographs, CT, and MRI scans are not intuitive enough, and it can be difficult to imagine 3D neuroanatomical structures when using 2D images as a starting point (Papa and Vaccarezza, 2013).

#### 1.2.4 New Alternative Ways of Teaching Anatomy

The move from in-depth anatomy courses to integrated and system-based curricula, as well as small number of anatomy lecturers coupled with limited teaching time creates a strong need for affordable, but still effective alternatives to cadaveric dissections. Plastination, medical imaging, educational computer software and blended learning can be considered such alternatives (Estai and

### Bunt, 2016).

Electronic learning resources that employ 3D technology and Virtual and Augmented Reality (VR and AR) can be considered a good alternative to traditional methods of teaching anatomy (i.e., cadaveric dissections, prosections, textbooks, two dimensional illustrations and medical imaging such as MRI and CT) (Biassuto, Caussa and Criado del Río, 2006; McLachlan and Patten, 2006; Estai and Bunt, 2016; Ekstrand et al., 2018; Bogomolova et al., 2020; Mendez-Lopez et al., 2021). VR allows users to be completely immersed in the virtual environment, whereas AR lets users to see the real world with virtual elements overlaid on it (Kipper, 2013). AR overlays digital 3D models on the real world through the use of a camera and a screen, therefore allowing the user to interact with both real and virtual elements of the environment (Azuma, 1997; Azuma et al., 2011). It enhances the real world, but remains intuitive and easy to use (Azuma, 1997; Azuma et al., 2011; Kipper, 2013). AR can be viewed as "a middle ground between real and virtual worlds" (Kipper, 2013). Although this new technology on its own does not necessarily improve the educational process, a number of educators and researchers in the medical field share the view that dynamic and interactive media hold enormous potential for education and training (McLachlan et al., 2004; Biassuto, Caussa and Criado del Río, 2006; McLachlan and Patten, 2006; Estai and Bunt, 2016; Mendez-Lopez et al., 2021).

Unlike cadavers, VR and AR-based 3D resources do not require highly complex procedures such as embalming, and there is no need for expensive storage logistics and infrastructure. VR and AR-based learning model also offers advantages of portability and flexibility: it allows students to study at university campuses or at home at their convenience (Estai and Bunt, 2016). Besides, 3D technology can be accessed by students any time, any place, and for as long as required, whereas cadavers are only available for limited periods of time at the university facilities (Berrios Barillas, 2019).

While there are some concerns being raised about the lack of haptic responses in AR-based applications, Kugelmann et al. (2018) demonstrated that it did not prevent students from acquiring excellent understanding of three-dimensional anatomy. There is also evidence suggesting that AR-based applications increase students' motivation and fuel their interest in learning anatomy, mainly due to the interactive aspect of these teaching resources (Kugelmann *et al.*, 2018; Weeks and Amiel, 2019).

AR has the potential to make educational environments "more productive, pleasurable and interactive than ever before" (Lee, 2012; Weeks and Amiel, 2019; Mendez-Lopez *et al.*, 2021). Applications simulating virtual dissection can allow students to carry out the same action repeatedly, honing their skills, something that is impossible with an actual cadaver (Washmuth *et al.*, 2020). Unlike physical models and cross-sections, AR-based applications allow students to

virtually pull apart and put back together anatomical structures, which significantly improves their understanding of the material (Henssen *et al.*, 2020). It is proven that simulation-based learning model is more efficient than the traditional master-apprentice teaching model, it flattens the learning curve, reduces number of clinical errors, which in turn leads to reduced healthcare costs (Oliveira and Figueiredo, 2019). AR-based educational apps used on mobile devices have potential to increase students' productivity by sending task reminders and employ other ways to redirect learner's attention. Mobile technology also means that learners can communicate and collaborate with each other (Wu *et al.*, 2013).

Although 3D learning resources tend to be more effective than 2D alternatives (Mayer and Moreno, 2003), such as textbooks and 2D images, there are still some pitfalls that must be taken into account. For example, if learning resource is overloaded with information, it can confuse the user and reduce quality of learning. However, most of the VR and AR-based applications allow interaction, which can mitigate this risk (Mayer and Moreno, 2003). However, interactive elements alone do not make a 3D-based learning tool more accessible to users: poorly designed interface can take user's attention away from the task of learning the concepts presented in the application, and therefore increase cognitive load, rather that relieve it. Therefore, it is paramount that the interface is designed with human computer interaction concepts in mind. (Hegarty, 2004). Wu et al (2013) warn of potential risk of cognitive overload for users due to "large amount of information they encounter, the multiple technological devices they are required to use, and the complex tasks they have to accomplish". There is also evidence suggesting that students with weaker visual-spatial abilities are likely to experience difficulties with rotating 3D models to a specified view (Bogomolova et al., 2020). Other challenges associated with the novel teaching methods include providing dedicated space for AR education, providing educational and IT support for these sessions, and providing additional capital for the required devices and software (Weeks and Amiel, 2019).

Thomas et al. (2010) presented Bangor Augmented Reality Education Tool for Anatomy (BARETA), a system that combines AR technology with 3D models, providing students with haptic elements as well as with visual. The main goal of the project was to develop an interface that is more intuitive that the traditional setup, which uses mouse and keyboard. Thomas et al. suggest that AR as a teaching method offers a lot of advantages over other resources. One of them is opportunity for collaboration, as the AR environment can be shared. "*AR can also provide the user with effective positional cues because the surrounding real environment is constantly visible*", add Thomas et al. Finally, AR offers simple and intuitive interface that is easy to master (Thomas, John and Delieu, 2010). Ruthberg et al. (2020) consider Mixed Reality (which could be considered a more advanced form of AR) the best teaching resource for these reasons. Mixed Reality, which

merges real and virtual environments (similar to AR), offers users opportunity to collaborate, simple interface, plus all the advantages provided by VR, but without its shortcomings, such as isolation and mild dizziness experienced by some users. Overall discomfort due to use of AR as compared to use of VR is much lower (Mendez-Lopez *et al.*, 2021).

Cadaveric dissections still play a very important role in teaching anatomy, however, it should be acknowledged that new initiatives such as that of Visible Human datasets could potentially supplement, or even replace completely this traditional way of teaching anatomy (Motsinger, 2020). Azer and Eizenberg (2007) studied attitudes of first and second-year medical students towards cadaveric dissections. The results demonstrated that the first year students ranked cadaveric dissection as more effective than the second year students, who preferred textbooks as their main learning resource. However, these new methods of teaching did not influence either first or second year students perceptions of cadaveric dissection, and were seen as additional resources at most (Azer and Eizenberg, 2007). There is some evidence suggesting that learning style of a student can play important role in determining the end result from using computer-based study materials. Those students who are self-disciplined and able to take charge of their own learning can benefit more from online-based 3D resources, whereas students who prefer more structured and supervised learning mode are disadvantaged (Mathiowetz, Yu and Quake-Rapp, 2016). The shift towards students taking charge of their own learning process and the greater use of an individual online learning spaces outside of the classroom, create a need for effective 3D-based learning resources (Chariker and Pani, 2002; Mathiowetz, Yu and Quake-Rapp, 2016; Sotgiu et al., 2020). There is evidence that suggests that 3D-based learning is more effective when paired with other educational materials (e.g., 2D illustrations and textbooks), as it allows better understanding of the topography and spatial arrangements of the neuroanatomical structures in relation to each other (Weeks and Amiel, 2019; Sotgiu *et al.*, 2020).

#### 1.2.5 Digitally enhanced neuroanatomy – Can novel technology alleviate Neurophobia?

As mentioned above, there is a body of evidence that suggests that AR can be a useful tool for enhancing students' experience of learning neuroanatomy (Weeks and Amiel, 2019). Weeks and Amiel (2019) also observed that AR-based applications have received highly positive feedback from the students who took part in the study. One of the students participating in study spoke of the AR app as "single most helpful anatomical learning tool I have used". 3D-based applications can be invaluable tools for introducing students to neuroanatomy in a fun, engaging way, for facilitating the learning process, and for improving long-term information retention (Chariker and Pani, 2002).

Kockro et al. (2015) compared students' results in a Multi Choice Question Exam. Students in the control group were learning about the third brain ventricle using Microsoft Power Point presentation featuring 2D images and verbal descriptions and explanations. The other group was using VR-based application featuring multi-layered 3D model of the brain. The results of the study demonstrated significantly better learning outcomes for the VR group, which confirms the hypothesis that spatial orientation skills are crucial for successfully mastering neuroanatomy. Kockro et al. suggested that, considering limited access to cadavers and overall difficulties associated with practice of dissections, VR resources like the one in the study could be considered a good alternative to traditional ways of teaching neuroanatomy (Kockro *et al.*, 2015).

A study, conducted by Stepan et al. (2017) demonstrated that a VR resource featuring 3D models of the neuroanatomical structures could be as effective as the traditional learning resources such as textbooks and anatomical atlases for preparing students for exams. Moreover, the VR application was rated higher than the traditional learning resources in several subjective measurements: engagement, enjoyment, usefulness, and learner motivation. Although Stepan et al. (2017) acknowledge that previous research involving usage of 3D models, VR and AR for teaching anatomy had mixed results, they pointed out that majority of these studies were based on using older and less advanced equipment which did not allow for a fully immersive experience. It was also found that, although there is no significant difference in retention of the newly learned material, the VR group rated their studying experience as much more enjoyable and engaging as compared to the control group. Moreover, the VR group had significantly higher motivation score as measured by Instructional Materials Motivation Survey (IMMS). It is important to note that both VR and control groups had high base level of anatomy knowledge prior to the experiment. Considering increasing shortage of cadavers and other challenges associated with the cadaveric dissections, VR seems to be a very attractive alternative. As technology develops and becomes more accessible to wider public, popularity of VR applications will only increase (Stepan et al., 2017).

Ekstrand et al. (2018) conducted another research that demonstrated that VR application featuring 3D models of the brain improved first and second year medical students' engagement level, motivation, and increased knowledge retention. They also reported that neurophobia among students diminished significantly. Ekstrand et al. suggested that use of VR technology could be extended into more specialised medical fields such neurology and neurosurgery, rather than being restricted to the undergraduate curricula (Ekstrand *et al.*, 2018). VR and 3D technology, although still in its infancy, has great potential for improving learning experience for the medical students and neurosurgeons alike, suggest Ekstrand et al. (2018).

A study conducted by Bohl et al. (2019) suggested that use of high-fidelity 3D models might even

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be superior to the traditional learning resources that are currently being used for teaching anatomy to trainee neurosurgeons: "*Resident and attending neurosurgeons subjectively believe that high-fidelity synthetic models were superior to cadavers as a surgical skill teaching platform*". These results may suggest that the shift from cadavers to computer-generated learning tools is likely to happen in the near future (Bohl *et al.*, 2019).

Peterson and Mlynarczyk (2016) suggested that "*a combination of dissection and computer assisted digital teaching media may provide an optimal learning platform for anatomy students*". In their study they examined the effect of AR on the level of retention of the newly learned information by students with different levels of knowledge prior to experiment and with varying perceptions of AR (Peterson and Mlynarczyk, 2016). The results of the study demonstrated that the 3D resources improved students' understanding significantly and improved their performance during exams. Although Peterson and Mlynarczyk admit that multitude of studying materials could have influenced the results, they made clear that further studies are needed. Interestingly, students who had lower marks in previous examinations, demonstrated better performance after using AR, just like the students who had higher marks prior to the experiment. Peterson and Mlynarczyk argue that AR-based 3D applications could give advantage to the students using them over those who do not have access to such technology. It is worth mentioning that students who had better spatial abilities benefited from using 3D materials more than those who struggled with tasks involving spatial orientation (Peterson and Mlynarczyk, 2016).

Although there is still no definite answer of whether 3D technologies, VR and AR are more effective than traditional methods such as dissections, prosections, 2-dimensional images and textbooks, there is a lot of evidence showing that some anatomical concepts that require higher degree of spatial awareness (e.g., mental rotation and mental imagery) are easier to master using 3D resources (Hoyek *et al.*, 2014; Ekstrand *et al.*, 2018; Bogomolova *et al.*, 2020; Sotgiu *et al.*, 2020; Mendez-Lopez *et al.*, 2021). It is also worth mentioning that most of the recent research is focused on exploring VR, and Gerup et al. point out the lack of research done on use of AR in medical education. All the studies that have been reviewed above demonstrated many educational benefits of AR and MR resources as compared to the traditional teaching methodologies (Gerup, Soerensen and Dieckmann, 2020).

The use of mobile apps that feature AR to assist students with learning neuroanatomy appears to be a very attractive idea, especially considering that the vast majority of the UK students own at least one mobile device (smartphone or tablet). It means that AR technology is easily accessible for them, allowing an opportunity to access learning materials even when they are not on campus. The Covid-19 pandemic highlighted the need for flexible study opportunities, and educational mobile apps featuring 3D and AR elements can help to fill this gap.

## **1.3 Materials and Methods**

## 1.3.1 Materials

The mobile application featuring 3D and AR elements was created using three types of materials: data, hardware and software.

Data included the following: 1). an anonymised MRI scan of the brain which was used as a starting point for the 3D model; 2). Seamless texture that was later modified and applied to the model of the brain; 3). Fonts Liberation Sans and Avenir which were used in the app and in the PDF booklet.

Software included: 1). 3D Slicer, which was used for 3D visualisation and manual segmentation of the MRI dataset; 2). 3D Studio Max, which was used to optimise the mesh by reducing the number of polygons in the model and for retopology; 3). Maya was used to apply the UV maps to the model; 4). Unity 2019, Visual Studio Code, and AR Core were used to develop the application; 5). Adobe Suite (Photoshop, Illustrator, Fresco, inDesign) was used to design the PDF booklet, to create AR targets (illustrations), to modify the textures, and to design the poster that was used to recruit the participants for application testing; 6). Google Surveys were used to design the surveys that were used during testing the application with the participants.

Hardware included: 1). The laptop (Acer Swift 5) that was used for segmentation, modelling, design and development of the application; 2). The tablet device (Samsung Galaxy S5) that was used to test the application. Running Android 10 (Pie); 3). The graphics tablet with stylus pen (Wacom Intuos Graphic Tablet), was used for creating 2D illustrations, textures and UI elements.

Software	Use	Publisher
3DSlicer 3DSlicer	3D visualisation and manual segmentation of medical imaging data	Available at: www.slicer.org
3D Studio Max	3D modelling software, was used to reduce number of polys and retopology	Autodesk, Inc., New York, USA (Autodesk, 2021) <u>Available at:</u> <u>www.autodesk.co.uk</u>
Maya	3D modelling software, was	Autodesk, Inc., New York,

Table 1: List of software used during development of the project:

	used to apply UV maps to the models	USA (Autodesk, 2021). Available at: <u>www.autodesk.co.uk</u>
Unity 3D	Game engine software, was used to create the application	Unity Technologies, California, USA (UnityTechnologies, 2021) Available at: unity3d.com
Visual Studio Code Visual Studio Code	Code editor, was used to write C# scripts.	Visual Studio Code, Microsoft, 2021. Available at: code.visualstudio.com
AR Core ARCore	A software development kit for building AR-based applications using Unity 3D	Google, Inc., California, USA Available at: developers.google.com/ar
Adobe Photoshop PS	Program used for editing textures	Adobe Systems, Inc., California, USA Available at: adobe.com
Adobe Illustrator	Program used for creating storyboard, moodboard, UI elements and workflow diagrams.	Adobe Systems, Inc., California, USA Available at: adobe.com
Adobe Fresco	Program used for creating illustrations, including AR targets	Adobe Systems, Inc., California, USA Available at: adobe.com
Adobe InDesign	Program used for creating booklet	Adobe Systems, Inc., California, USA Available at: adobe.com

Table 2 Hardware used to create the application:

Hardware	Use	Manufacturer
Acer Swift 5	The laptop that was used for	Acer Inc.(2021)
acer	segmentation, modelling, design and development of	
	the application	
Samsung Galaxy Tab S5	The tablet device that was	Samsung Group, Seoul,
	used to test the application.	South Korea (Samsung,
	Running Android 10 (Pie)	2021)

samsung Galaxy		
Wacom Intuos Graphic Tablet Wacom	A graphics tablet with stylus pen, was used for creating 2D illustrations, textures and UI elements	Wacom Co., Ltd, Kazo, Japan (Wacom, 2021)

Table 3 Data used in the application:

Data	Use in the application	Publisher
R R R R R R R R R R R R R R R R R R R	It was used for performing segmentation of the brain structures	Available at: www.slicer.org
Liberation Sans	The font that was used for creating labels in 3D scene of the application. One of the default fonts in Unity	Unity Technologies, California, USA (UnityTechnologies, 2021) Available at: unity3d.com
Avenir Font abcdefghijklmnopqrstuvwxyz ABCDEFGHIJKLMNOPORSTUVWXYZ Avenir is a Geometric Sans Serif typeface.	The font that was used in the accompanying booklet.	Available from: www.dafont.com
	The seamless texture that was used for the brain model	Available from: https://3dtextures.me/tag/bra in/

#### 1.3.2 Methods

The purpose of this mobile application is to provide users with the opportunity to review anatomy of the brain using 3D and AR technology together with the labelled 2D illustrations of the six different brain structures. A PDF booklet containing illustrations serving as AR targets was designed to accompany the application. Apart from the AR targets it includes brief description of the featured neuroanatomical structures, as well as the instructions on how to download, install, and use the app. The diagram shown on Fig 1 explains the workflow of the development.

# Fig 1: the workflow followed during development of the application and relationships between different parts of the development.

Mobile devices (smartphones and tablets) are quite ubiquitous in the UK, which means that an interactive educational mobile application can be considered an easily accessible and affordable learning resource.

AR and 3D technology makes the process of learning neuroanatomy more user-centred, as the user can actively interact with the content, instead of passively consuming it. Due to neuroanatomy being a highly visual subject and requiring learners to have good spatial abilities in order to understand how different structures relate to each other, the inclusion of different modes of visual representation of the brain structures, such as an interactive 3D model, 2D illustrations and labelled MRI data has potential to provide users with learning environment that addresses the unique challenges that this subject presents.

During planning stage of the application development process, a MoSCoW diagram was created to weigh up the importance of each aspect of the application (Fig 2). This helped to prioritise tasks, to structure the design process and to ensure good time management.

Fig 2: MoSCoW diagram was used during planning stage to prioritise tasks and assist time management.

Initially, the development idea included adding head and skull models to the 3D scene, but due to high polygon count it would create in the scene, the decision was made against using these elements and focus solely on the brain anatomy.

A storyboard (Fig 3a) was created to visualise the scenes and structure of the user interface (UI). The application was to consist of AR, 3D and 2D scenes. A short quiz was added to give users an opportunity to test their acquired knowledge. All the scenes have a button which takes the user back to the main menu.

The idea behind the Moodboard (Fig 3b) was to visualise ideas for the AR targets and for the overall feel of the application. Because the AR targets must have high contrast levels in order to function as intended, decision was made to make images black-and-white. This influenced the overall design of both application and booklet. Colour was used for the UI elements and backgrounds.

# *Figures 3a, 3b: Storyboard and Moodboard were created to outline application setup and develop visual aesthetic of the application and the booklet.*

A simple, minimalist interface was a high priority for this application. Backgrounds and UI elements were designed using calm, muted colours (as shown on Fig 4) that would not distract user's eye from the visual content of the app. Most mobile devices tend to have limited screen space, therefore, UI was designed to be as laconic and as intuitive as possible.

Fig 4: Colour palette was designed to ensure that all parts of the application (UI, backgrounds, illustrations) and the booklet maintain consistency.

Backgrounds for the scenes of the app were designed in Adobe Photoshop, using shades from the colour palette, and the AR targets were hand drawn in Adobe Fresco and Adobe Illustrator. The app icon (Fig 5a) was designed in Adobe Photoshop in accordance with specifications listed on the website for Android developers (*Google Play icon design specifications* | *Android* <u>*Developers*</u>): size 512 \* 512 px and using RGB colour space. Extra space around the edges was left to allow for the crop which would occur during application built process.

## Figures 5a and 5b: the app icon and loading screen were designed in Adobe Photoshop.

### 1.3.2.1 Model Development

The 3D model of the brain was created using sample MRI dataset which is included in the opensource software 3D Slicer. This decision was influenced by the fact that this dataset is anonymised and therefore there is no ethical issues associated with using it. The segmentation in 3D Slicer had to be performed manually, because individual parts of the brain had to be represented as separate models. To facilitate the process, Laplacian Sharpening Image Filter (Figures 6a and 6b) was applied beforehand to increase the contrast levels of the dataset.

## Figures 6a and 6b: MRI dataset before and after applying Laplacian Sharpening Image Filter.

### Figures 7 and 7b: The segmented MRI dataset and the list of segments.

The finished models were then exported as OBJ files from 3D Slicer and imported into 3DS Max 2022 for optimisation. The original number of polygons was extremely high and had to be reduced to make the models usable in Unity. ProOptimizer modifier was applied to reduce polycount, followed by the Retopology tool to optimise the mesh (Figures 8a and 8b).

# Figures 8a and 8b: mesh before and after applying ProOptimizer and Retopology tools. The polycount was reduced from 566,640 to 45,632.

The next stage of the model development was optimising and applying textures. UV maps were based on seamless textures which were accessed on 3Dtextures.me/tag/brain/. The albedo map was altered in Photoshop to make it more realistic. Separate textures were created for internal parts of the brain and applied in Maya. Normal maps were also adapted and later added in Unity 3D.

### 1.3.2.2 Application Design

The application was developed in Unity 2019.4.32f1, a game engine software. The application was designed to include AR scene, 3D scene and 2D scene, as well as a short quiz to allow user to test their knowledge (Fig 9). There is no set order in which user should interact with the scenes: they are all easily accessible from the main menu and are completely independent from each other. Both AR and 3D scenes feature interactive 3D model of the brain. 2D scene features 2D illustrations and bullet points about each brain structure included in the model, plus annotated MRI slices. This is aimed to give user opportunity to review the material even if they do not have the booklet to hand. The quiz can be accessed from the main menu and user can stop quiz at any time and return to the main menu in case they want to get back to learning, or to quit the quiz completely.

Figure 9: This diagram demonstrates the scenes included in the application and relationship between them.

The AR scene relies on the illustrations from the PDF booklet as markers to trigger the 3D models of the brain structures. The scene features six structures with corresponding 2D illustrations: cortex,

brain stem, cerebellum, ventricles, basal ganglia and anatomical structures of the limbic system. The booklet was created using Adobe InDesign (Fig 10). All the illustrations and design elements are created in Adobe Photoshop, Illustrator and Fresco. Font Avenir was selected for its clean and modern design.

Fig 10: The PDF booklet was created using Adobe InDesign.

The AR environment was developed using AR Foundation (version 4.1.1). AR Core XR Plugin and an updated Gradle version (v.6.8.3) were imported into Unity project as the application is intended for Android mobile devices.

The 2D scene (Fig 11) was created to allow the user to revise neuroanatomy even when they do not have access to the booklet at the time, for example, when they are learning on the go. The menu features six panels with labelled illustrations and MRI scans displaying the neuroanatomical structures featured in the AR scene. The user can learn more about each brain structure by clicking on the "Learn more" button.

*Fig 11: The 2D scene menu featuring a row of six buttons linking to the panels containing labelled illustrations and MRI scans.* 

*Figures 12a and 13b: Panels featuring labelled illustration, MRI scan and brief description of the cerebrum.* 

The 3D scene features a complex interactive model of the brain. User can explode the model using slider, zoom in and out using the second slider, and rotate it by swiping the screen sideways. The model is composed of thirteen individual parts representing different neuroanatomical structures. Exploding functionality allows user to view different parts of the brain individually and to appreciate their spatial relations to each other. Initially, due to bilateral symmetry of the brain, exploding was not as even as intended. This challenge was overcome by using several dummy objects, which were then spread evenly with the brain structures attached to them. This workflow ensured that all the brain parts remained positioned correctly in relation to each other.

Figures 13a and 13b: brain model in default and in zoomed-in exploded state.

Textures were imported into Unity and adjustments were made to suit individual brain parts. Albedo map provided colour, whereas Normal map allowed to enhance realism of the model by making gyri and sulci appear more pronounced, while maintaining low polycount of the models. Albedo maps for smooth structures such as brainstem were adjusted in Photoshop to appear slightly lighter.

### Figures 14a and 14b: Temporal lobe before and after applying Normal Map.

Figure 15: Settings of the maps on the example of the temporal lobe.

*Figures 16a, 16b, 16c, 16d: Original Albedo Map (16a), Cortex Albedo Map (16b), Albedo Map used for other structures (16c) and Normal Map (16d) used to give cortex more realistic look.* 

To add finishing touches to the application and to make it look more polished, a number of post processing visual effects were applied (Figures 17 and 18). Ambient Occlusion was added to make lighting appear more natural. Vignette effect was employed to create a slight gradient to the background and give the scene a more complete and finished look. Colour grading was used to add a slightly cooler tone to the scene. Saturation was tuned down to give the brain model more realistic appearance. Contrast was increased and a very small amount of grain was added. Finally, motion blur was applied to make exploding and rotating actions look more polished).

Fig 17: The Post Processing package was imported from Package Manager.

Fig 18: Ambient Occlusion, Vignette, colour correction, Motion Blur, and Grain effects were added

Figures 19a and 19b: 3D scene before and after applying post processing effects.

The quiz scene was added to give users opportunity to test their knowledge of the material. It was designed to randomly select seven questions from the pool of ten. A small tick appears in a box if the correct answer is selected. Depending on whether the user selects correct or wrong answer, semi-transparent green and red panels appear, overlaying the screen. If the incorrect answer is chosen, the user can either proceed to the next question, or return to the main menu, if they wish to review the material.

### Figures 20a and 20b: Correct and wrong answer screens

A score panel was added to show how many questions were answered correctly.

Figure 21: A score panel that appears when user finishes the quiz.

### **1.4 Evaluation**

An experimental approach was developed to evaluate educational value and usability of the app. This approach had two aims:

1) to find out whether the app can help users to acquire knowledge of neuroanatomy;

2) to evaluate the degree of usability of the app.

To take part in the study participants were required to be over 18-year-old and have access to an Android mobile device, a tablet or a smartphone, running at least Android 10 (Pie). They were not required to have any prior knowledge of neuroanatomy before testing the app. All the participants who took part in this study were guaranteed complete anonymity and no data that could be used to identify them (e.g., e-mail addresses) was collected.

## **1.4.1 Participants**

A total of twelve participants contributed to this study (seven females and five males). Six (50%) participants held a Bachelor degree, three (25%) had a Master degree, one (8.3%) had completed some form of higher education, one (8.3%) only finished high school and one (8.3%) participant had no formal education being stated. Seven (58.3%) participants had beginner level of neuroanatomy knowledge, four (33.3%) had no knowledge of brain anatomy at all, whereas one (8.3%) participant stated to have advanced knowledge. All twelve participants owned at least one mobile device. The majority of the participants use their mobile devices for learning purposes: six (50%) do it sometimes, and five (41.7%) people picked option "Often". One (8,3%) participant stated that they do not use their device for learning. Nine (75%) participants have not used AR on a mobile device, however, three participants (25%) did.

Fig 22: Most of the participants had some form of higher education.

## 1.4.2 Apparatus

The application that was offered to the participants for testing is designed to be used as a learning tool by anybody who wishes to gain or improve their knowledge of neuroanatomy. The application can be installed on any mobile device running Android 10 (Pie) or above. The AR functionality featured in the app relies on the accompanying PDF booklet.

## 1.4.3 Procedure

The study was advertised on the XR Distributed Research Network (<u>www.xrdrn.org</u>) and was shared on social media (e.g. <u>www.linkedin.com</u>, <u>https://twitter.com</u>). After completing consent and personal information forms, the participants were asked to fill a pre-test questionnaire. They were then asked to download and install the application on their Android mobile device, as well as the PDF booklet from a Google Drive link. After using the app on their mobile, participants were required to answer the questions from the pre-test neuroanatomy quiz but reordered into a separate post-test questionnaire.

Fig 23: An advert was created to recruit participants on XR Distributed Research Network.

### 1.4.4 Data Analysis

The participants were required to download and install the application on their mobile device using link provided. An accompanying PDF booklet could be accessed using the same link.

To assess participants' acquisition or development of knowledge of neuroanatomy, they were asked to complete a 10-question quiz before and after testing the app, along with a set of 10 questions from the standardised usability assessment, the System Usability Scale (SUS) (Brooke, 1996).

The data analysis of the pre- and post-testing neuroanatomy questionnaires was performed in PSPP software using Mann-Whitney U Test comparing mean values. Mann-Whitney test is commonly used to compare the differences between two independent samples in non-normally distributed dataset. The SUS was calculated in the following steps:

• X = Sum of the points for all odd-numbered questions - 5

- Y = 25 Sum of the points for all even-numbered questions
- SUS Score =  $(X + Y) \times 2.5$

The odd-numbered questions are written in the positive tone, so response "Strongly Agree" receives 10 points, whereas response "Strongly Disagree" receives 0. This is reversed for even-numbered questions: response "Strongly Agree" receives 0 points, and response "Strongly Disagree receives 10.

### 1.4.6 Results

### **Knowledge acquisition**

The pre-test questionnaire consisted of ten single-choice questions, seven of which were accessible through the app.

The post-test questionnaire consisted of the same questions as in the pre-test one, but presented in different order. This allowed establishing whether the participants' knowledge of neuroanatomy

improved after interacting with the app. Results of the post-test quiz were significantly better than the results of the pre-test, which reflects improved knowledge of neuroanatomy amongst the participants.

Table 4: Test results demonstrate significant improvement of participants' knowledge of neuroanatomy

Figure 24: Neuroanatomy quiz results before and after testing the application.

## **Usability Analysis**

The usability questionnaire consisted of the standardised ten questions of the SUS (Brooke, 1996) and additionally four questions to provide further insights on the various aspects of the application such as realism of the 3D model, user-friendly interface, and educational value. The SUS was chosen for usability evaluation due to the following reasons: 1). It is considered an industry standard, 2). It can be used with a small number of participants while providing reliable results, 3). It is effective in differentiating between usable and unusable systems (Brooke, 1996). The application scored very well on SUS: its usability scale was reported at 82.2, which is above the typical SUS benchmark (68) by 13.79 points. As Table 3 demonstrates, the application would receive an A mark. One of the participants rated usability of the app lower due to problems they encountered while using it: the visuals were "stretched". This would be due to the application being used on a rather narrow smartphone screen, instead of on a larger tablet screen.

Table 5: The results of the Usability Questionnaire.

Figure 25: Graph demonstrating usability score of the application.

Table 6: System Usability Score (SUS) used to determine the grade of the application.

The additional four questions that were added to the standardised SUS questionnaire to explore the following points:

- Realism of the 3D model of the brain
- Whether or not the participants felt their knowledge of neuroanatomy improved after using the app
- Whether or not being able to explore anatomical structures of the brain in both 3D and 2D

scenes improved the participants' understanding of the subject

• Whether or not the application was engaging enough and fun to use

Most of the participants thought that the 3D model looked realistic and felt that interacting with it improved their knowledge and understanding of neuroanatomy. A lot of participants made highly positive comments on design of the accompanying booklet and on the style of the illustrations. Adding more questions to the usability survey, such as the questions about realism of the 3D model and effectiveness of the app as a learning tool, made the survey more tailored and therefore more effective and useful for gathering user feedback in the specific context of this study. The results of the survey can be invaluable for making future improvements in the app design. *Figure 26: Self-Assessment of Usability*.

## **1.5 Discussion**

### 1.5.1 Design and 3D Modelling Processing

A MoSCoW approach was undertaken to identify the major functionalities of the app and plan for efficient project management. It was a useful approach, however it did not highlight more fine requirements of the project. The next steps were moodboard and storyboard creation, which helped to present the finalised design provided guidance throughout the development stage of the project.

The 3D model of the brain was created using 3D Slicer, 3DS Max, and Maya. The first stage of the process, segmentation, was completed in 3D Slicer. As the desired outcome was a complex model consisting of several separate parts, segmentation had to be performed manually due to different neuroanatomical structures having similar density. Manual segmentation was a time-consuming process but was nevertheless completed within the timeframe allocated. Completed segmentations were then exported from 3D Slicer as models in obj format. They were then imported to 3DS Max, where polycount, originally very high, was significantly reduced using the automatic ProOptimizer tool. Using ProOptimizer allowed to save a lot of time, however some manual adjustments were required to further optimise the mesh. Automatic Retopology tool was then applied to make the mesh suitable for texturing. This tool was highly effective, although, just like ProOptimizer, it required some additional touches. Although the 3D model of the brain as a whole was incredibly complex, its individual parts were represented as relatively simple shapes. This allowed Pro-Optimizer and Retopology tools to dramatically reduce polycount of each part of the model, but still maintain anatomically correct shape and look of the brain structures. Due to carefully performed segmentation, the meshes had no major issues. A small number of floating vertices were welded together, and a small number of holes were closed manually, before applying Pro-Optimizer and Retopology tools, so the whole modelling process went smoothly. Texturing using seamless textures was completed in Maya and Unity. Cortex lobes and cerebellum lost some detail during polygon reduction and retopology processes, but this was compensated by applying normal maps in Unity. This allowed to keep number of polygons low, while still maintaining realistic look of the model.

### **1.5.2** Critical Reflection about Experimental Outcomes

Neuroanatomy is a discipline that many students find extremely complex and difficult to grasp (Edwards-Bailey et al., 2021). The application has shown to be a successful medium for improving the participants' knowledge of neuroanatomy and proven to be a fun and engaging tool for learning the basics. The collated data clearly demonstrates significant improvement of the participants' neuroanatomy knowledge after using the app. However, the base level of knowledge of the participants varied significantly and it needs to be taken into consideration. In addition, due to time restrictions, it was impossible to assess whether the application improves knowledge retention on a longer period of time. Then, the uncontrolled nature of the experiment design can also be considered problematic. Effectively, seven questions from the questionnaires were issued from the quiz within the application. There might be possible bias from participants remembering from their answer when using the quiz. Consequently, further testing is needed to assess long term retention of knowledge. Also, due to the nature of the experiment where it was impossible to observe the participants, there is a possibility that the participants could have been consulting additional resources to help with the post-test questionnaire.

The application scored high in usability testing, which was above the benchmark rating of 68. The data obtained shows that the vast majority of the participants considered the application to be intuitive and easy to use. All the participants agreed that being able to see brain in both 2D and 3D modes improved their understanding of its anatomy. The accompanying PDF booklet also received highly positive feedback regarding its design and educational value. The negative feedback provided by one of the participants resulted from the application being used on a smartphone rather than a tablet, which lead to some visual elements of the app being distorted.

Further testing with larger number of participants would benefit this study by allowing to consolidate and confirm the results. Observing the participants' interactions with the app would also be helpful for improving evaluation of the knowledge acquisition and understanding of the strong and weak aspects of the application design (e.g., UI and UX).

## **1.6 Future Development**

Although the research aim was met, there are still a number of improvements that could be implemented in the future.

The quiz scene could be improved in a number of ways. The pool of questions could be larger to give the user more opportunity to test and improve their knowledge of the material. The gradient overlay (green for correct answers and red for the wrong ones) can be problematic for users suffering from red-green colour blindness. The text labels "Correct!" and "Incorrect!" partly alleviate this problem, however, the interface still might be perceived as unintuitive by users with red-green colour vision deficiency.

Several participants mentioned that they would prefer 3D models in the AR scene to be more interactive. The 3D scene received very positive feedback, however, one of the participants suggested that pop-up windows appearing when individual brain structures are clicked to provide user with more information would be very helpful. Another participant mentioned that they would like to be able to rotate 3D model in the 3D scene along X axis, as well as Y axis. They also reported distortion of the visuals when using the app on the smartphone, instead of the tablet.

Further testing with larger number of participants and for a longer period of time is required to validate the results. Observing the way participants interact with the application would reveal a lot of shortcomings, as well as highlight the strong aspects of the app in respect of usability. Testing the application on a larger variety of devices with different screen sizes / ratios would allow to optimise the design further. Increasing the time of the experiment would benefit this study as it would allow evaluate long-term knowledge retention.

## **1.7 Conclusion**

Neuroanatomy is considered to be a challenging discipline that many students find extremely hard to master, and, as a result, might feel anxious and discouraged. A lot of anxiety associated with studying neuroanatomy stems from the inability of students to visualise anatomical structures of the brain in 3D. This presents a serious problem, considering the high demand for such specialists (Sotgiu et al., 2020). This research aimed to fill that gap providing an educational mobile app for Android that could be used as an introduction to neuroanatomy. AR and 3D-based learning tools can potentially contribute to alleviating this problem. AR and 3D technologies are commonly

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perceived more engaging and enjoyable than traditional learning tools, such as textbooks (Kugelmann *et al.*, 2018; Weeks and Amiel, 2019). An interactive AR and 3D-based app for Android-based mobile devices was developed during this project. The application allows user to interact with anatomically accurate 3D model of the brain in AR and 3D modes, as well as explore labelled 2D illustrations and MRI scans, featuring different anatomical parts of the brain. The accompanying booklet received highly positive feedback from the participants and was perceived as a useful learning aid as well.

The resulting application was successful at improving users' knowledge of neuroanatomy, as well as their experience with this challenging section of anatomy, through experimentation. Further developments of this app should be undertaken to increase its educational value for the users. Feedback and suggestions provided by the participants who took time to test the application should be implemented in these developments.

Although this application still requires some adjustments and refinements, it can be used at this stage as a resource for learning and reviewing anatomy of the brain. Nevertheless, more testing is indeed needed to consolidate encouraging experimental outcomes results.