Development of a 3D Printed Neuroanatomy Teaching Model, University of Ottawa

Safaa El Bialy, Robin Weng, Alireza Jalali

Faculty of Medicine, University of Ottawa, Ontario, Canada

ABSTRACT

Gross anatomy is seen as one of the basic bodies of medical knowledge. Likewise, neuroanatomy is foundational to clinical neurosciences. However, neuroanatomy is different from gross anatomy due to the complexity of the central nervous system, and the fact that some of its structures cannot be dissected or demonstrated in anatomy cadaveric lab. The use of anatomical models in medical curricula has been reported as an effective tool in anatomy learning. They have been used to replace cadaveric material when the latter is difficult to acquire, or when the anatomical structures cannot be dissected (for instance the brain ventricles). Moreover, anatomic models allow leaners to visualize the structures in a 3-dimensional modality. The goal of this study was to create a 3D printed neuroanatomy model in order to complement the University of Ottawa anatomy models' library, and help medical students visualize the pathway of different nervous tracts on a 3D simulation model. To assist with this, 2D images of slices of the cerebrum, brainstem, and spinal cord sections were downloaded online to be imported to Adobe Photoshop CC 2015. The images were manually converted to black and white, and separated into different layers to export each component separately into Tinker CAD (online software). The different components were then assembled on Tinker CAD to create 3D printer compatible files. The files were printed using white ABS on a Replicator 2X MakerBot printer. Two survey questions (Likert style) were sent to students via Google docs to evaluate their satisfaction with the model.

RÉSUMÉ

L'anatomie macroscopique est connue comme une base de la connaissance médicale. De même, la neuroanatomie est la fondation aux neurosciences cliniques. Pourtant, la neuroanatomie est différente de l'anatomie macroscopique due à la complexité du système nerveux central, et le fait que quelques structures ne puissent pas être disséquées ou démontrées dans un laboratoire d'anatomie. L'usage de modèles anatomiques dans les programmes médicaux a été rapporté comme un outil efficace pour l'apprentissage de l'anatomie. Ils ont été utilisés pour remplacer le matériel cadavérique qu'on ne peut pas facilement acquérir, ou si la structure anatomique ne peut pas se faire disséquer (par exemple, les ventricules du cerveau). De plus, les modèles anatomiques permettent aux apprenants à visualiser les structures dans une modalité tridimensionnelle. Le but de cette étude comprenait de créer un modèle de la neuroanatomie imprimé en 3D, pour ajouter à la bibliothèque de modèles anatomiques de l'Université d'Ottawa, et assister aux étudiants de médecine à visualiser les différentes voies nerveuses dans un modèle de simulation 3D. Pour assister à cette tâche, des sections de lames 2D du télencéphale, du tronc cérébral, et de la moelle épinière ont été téléchargées en ligne pour être importés dans Adobe Photoshop CC 2015. Les images ont été converties à noir et blanc, et séparées dans des différentes couches pour exporter chaque composant séparément dans Tinker CAD (logiciel en ligne). Les différents composants ont ensuite été assemblés dans Tinker CAD pour créer des fichiers compatibles avec l'imprimant 3D. Les fichiers ont été imprimés en utilisant un ABS blanc dans l'imprimant Replicator 2X MakerBot. Deux questions de sondages (en style Likert) ont été envoyées aux étudiants par Google docs pour évaluer leur satisfaction avec le modèle.

UNDERGO MANGE MANUST MET ALL STARK SERVIDE MANUST MANUST MANUST MANUS AND AREADY AS A history that extends back through the centuries to Aristotle and Galen. In medicine, gross anatomy has been seen as foundational, one o medical school curriculum, the study of anatomy has a history that extends back through the centuries to Aristotle and Galen. In medicine, bodies of knowledge that must be mastered as part of medical training in order to apply the diagnostic and treatment skills

required for clinical competence (1). "Likewise, neuroanatomy has been seen as foundational to clinical neurosciences, and it is included in every North American medical curriculum," according to Mauteen & D'Eon (2). "Neuroanatomy is the cornerstone upon which is built an understanding of the nervous system and its disorders," according to Crossman (3).

Keywords: 3D Printing; Neuroanatomy; Innovation in Medical Education

RESEARCH

However, neuroanatomy is quite different from gross anatomy, and this is attributable to the complexity of the central nervous system (CNS), as well as the many structures that are difficult to dissect and demonstrate in the anatomy cadaveric lab (for example, the brain ventricles, the nervous tracts, etc.). Moreover, CNS lesions do not manifest with local signs and symptoms. Although this is also true of other organ systems, such as the cardiovascular system, the difference is the inaccessibility of the CNS to direct physical examination. For instance, a lesion in the dorsal column-media lemniscus pathway will manifest as loss of touch sensation below the level of the lesion and it will present in a different side of the body based on the location of the lesion along the tract (e.g. above or below the medulla). Therefore, for lesions of the nervous system there is the need for a certain level of mastery of neuroanatomy to associate a lesion with the exact structure in the nervous system that induced it.

Anatomical models have long been used in anatomy education to supplement or replace cadaveric material when the latter is difficult to acquire. From the 14th until 18th century in France, Germany and Italy, anatomy was studied with the help of ivory figurines made by artists. After the invention of plastic, new opportunities in the study of anatomy were developed. At the beginning of 20th century, anatomy lessons were taught using plastic models of organs (4). Gültiken stated that the subjects introduced by plastic models are easier to learn and comprehend, as formaldehyde may mask the finer details of the anatomical complex (5). Therefore, the use of threedimensional (3D) anatomical models is ubiquitous in medical education. They allow the user to move away from the clutter, discomfort, and complexity of a cadaveric dissection and further clarify characteristics or functions of an anatomical structure that are not readily apparent in situ (6).

One of the neuroanatomy objectives at the University of Ottawa is for the students to locate the different nervous pathways and identify the outcome of a lesion in any part along the different tracts. The nervous pathways are very fine structures that cannot be dissected or demonstrated in anatomy cadaveric lab, and they are not purchasable from the market as 3D models. To address this issue and allow students to better identify the tracts, clarify the interconnectedness of the nervous system and facilitate the "locate the lesion" diagnostic approach, a 3D printed neuroanatomy model exclusive to the University of Ottawa was created to complement its anatomy library.

METHODS

2D images of slices of the cerebrum, brainstem, cervical, thoracic, and lumbar spinal cord were downloaded online and imported to Adobe Photoshop CC 2015. The images were manually converted to black and white, which were then separated into different layers and exported separately into Tinker CAD (online software). The different components were then assembled on Tinker CAD to create 3D printer compatible files (stereo lithography STL format). The files were printed using white ABS on a Replicator 2X MakerBot printer in the Faculty of Medicine' Health Sciences library at the University of Ottawa (7). The printed pieces measured 5x4x0.5 cm, 8x4x0.5 cm and 10x8x1 cm for the spinal cord, the brain stem, and the cerebrum slices, respectively. The pieces were then mounted on metal rods, and wires were passed through to demarcate the spinothalamic tract, corticospinal tract, and dorsal column-medial lemniscus pathway (**Figure 1**). The 3D model was introduced to students in neuroanatomy sessions and was kept in the lab allowing student access at any time. After approval by the Ottawa Health Research Institute-Research Ethics Board (OHRI-REB), two survey questions (Likert style) with a consent letter were sent to students via a Google

Figure 1. 3D printed neuroanatomy model showing the corticospinal, spinothalamic and dorsal column-medial lemniscus tracts

RESEARCH

docs to evaluate their satisfaction with the model. The overall response rate to the survey was 43.8% (70 out of 160 possible students). Students responding to the survey were those who regularly attend the labs. 79% ($n = 55$) of the students stated that the 3D model helped them better memorize the pathway of the tracts at different levels of the CNS and 80% (n $=$ 56) stated that it enhanced their understanding of difficult neuroanatomy concepts (**Figure 2**).

Figure 2. Students' perception of the neuroanatomy model as an educational tool (Second year medical students at the University of Ottawa, n=70).

DISCUSSION

The best model for investigating human anatomy has always been the human cadaver itself, because, in most cases, all the parts are present in the correct arrangement, the fine membranous and facial elements are intact, and the presentation of structures (soft, hard, smooth, rough, dry, moist) is accurate. It is safe to say that, from the beginning of curiosity, early man investigated wounds and organs of their dead brethren (6). However, in today's regulated and socially conscious institutions, access to a cadaver may be limited through budgetary or social issues, or, even if a cadaver is available, presentation of the desired cadaveric anatomy may be confusing, such as that of the pelvic spaces and fascia. Further, sometimes the structures cannot be demonstrated in cadaveric labs such as the nervous pathways. These issues can be addressed with fabricated anatomical models. Recent technological advances in 3D printing have resulted in increased use of this technology in the medical field (1,8). At the University of Ottawa, anatomy is taught to preclerkship students on a system base (musculoskeletal, vascular, respiratory, renal, gastrointestinal, endocrine, reproductive and nervous systems). The labs start with 30 minute PowerPoint

presentation followed by a quiz of two multiple-choice questions. The students then spend an hour with their assigned tutors exploring the cadavers; the sessions are supplemented by the 3D plastic models. Neuroanatomy is taught to medical students in their second year of studies. It is a complex subject and it even has the reputation of the subject that students fear the most. Some of the neuroanatomical structures cannot be demonstrated in the anatomy cadaveric lab. This issue was addressed by creating a 3D printed model of the nervous pathways. A survey of two Likert style questions was then sent to students. The majority of students responding to the survey were satisfied with the model as they stated that it enhanced their learning and helped them better understand difficult neuroanatomy concepts. 3D printing is one technological advancement that may reduce the need for purchasing a large library of physical 3D anatomical models. These models provide versatility; they can be tailored to the desired learning objectives and to conform to learner characteristics. They offer a great advantage over static 2D images in terms of orientation and exploration of internal structures. Moreover, the advantage of printing the models using different colors allow better visualization of anatomical structures. The only limitation of this technique is that it can be time consuming depending on the size of the printed object.

CONCLUSION

Neuroanatomy is perceived as a complex subject and educators are encouraged to deliver it in a simplified, easy to understand fashion. The use of different instructional approaches allows students to successfully retain information. 3D printing has advanced tremendously over the past two decades, becoming fundamental in the development and construction of physical 3D anatomical models. Advantages of these models over cadaveric specimens include their application in many educational formats (lectures, online material, and print) in addition to being portable, non-perishable and cost effective. These models can be altered to enhance desired learning objectives or to conform to learner characteristics. They offer a great advantage over static 2D images in terms of orientation and exploration of internal structures. 3D printing as an educational tool is uniquely flexible in responding to the evolving environment, leading to improved student learning outcomes and more retention of information. Therefore, it is recommended to continue developing opportunities where 3D printing can supplement traditional learning approaches. One future directive would be the assessment of the use of 3D teaching tools on students' examination performance.

REFERENCES

- 1. Man PY, Griffiths PG, Brown DT, Howell N, Turnbull DM, Chinnery PF. The epidemiology of Leber hereditary optic neuropathy in the North East of England. The American Journal of Human Genetics. 2003;72(2):333-9.
- 2. Meyerson C, Van Stavern G, McClelland C. Leber hereditary optic neuropathy: current perspectives. Clinical Ophthalmology (Auckland, NZ). 2015;9:1165.
- 3. Carelli V, d'Adamo P, Valentino ML, La Morgia C, Ross-Cisneros FN, Caporali L, Maresca A, Loguercio Polosa P, Barboni P, De Negri A, Sadun F. Parsing the differences in affected with LHON: genetic versus environmental triggers of disease conversion. Brain. 2015;139(3):e17.
- 4. Sadun AA, Win PH, Ross-Cisneros FN, Walker SO, Carelli V. Leber's hereditary optic neuropathy differentially affects smaller axons in the optic nerve. Transactions of the American Ophthalmological Society. 2000;98:223.
- 5. Orssaud C. Leber's hereditary optic neuropathy. Orphanet Encyclopedia. 2003 Nov.
- 6. Abu-Amero KK. Leber's hereditary optic neuropathy: the mitochondrial connection revisited. Middle East African Journal of Ophthalmology. 2011;18(1):17.
- 7. Zhuo Y, Luo H, Zhang K. Leber hereditary optic neuropathy and oxidative stress. Proceedings of the National Academy of Sciences. 2012 Dec 4;109(49):19882-3.
- 8. Lin CS, Sharpley MS, Fan W, Waymire KG, Sadun AA, Carelli V, Ross-Cisneros FN, Baciu P, Sung E, McManus MJ, Pan BX. Mouse mtDNA mutant model of Leber hereditary optic neuropathy. Proceedings of the National Academy of Sciences. 2012;109(49):20065-70.
- 9. Carelli V, Rugolo M, Sgarbi G, Ghelli A, Zanna C, Baracca A, Lenaz G, Napoli E, Martinuzzi A, Solaini G. Bioenergetics shapes cellular death pathways in Leber's hereditary optic neuropathy: a model of mitochondrial neurodegeneration. Biochimica et Biophysica Acta (BBA)-Bioenergetics. 2004;1658(1-2):172-9.
- 10. Levin LA. Mechanisms of retinal ganglion specific-cell death in Leber hereditary optic neuropathy. Transactions of the American Ophthalmological Society. 2007;105:379.
- 11. Guy J, Qi X, Pallotti F, et al. Rescue of a mitochondrial deficiency causing Leber hereditary optic neuropathy. Annals of Neurology. 2002;52:534-542.
- 12. Qi X, Lewin AS, Sun L, Hauswirth WW, Guy J. SOD2 gene transfer protects against optic neuropathy induced by deficiency of complex I. Annals of Neurology. 2004;56:182-191.
- 13. Macmillan C, Johns TA, Fu K, Shoubridge EA. Predominance of the T14484C mutation in French-Canadian families with Leber hereditary optic neuropathy is due to a founder effect. American journal of human genetics. 2000;66(1):332.
- 14. Liu H, La Morgia C, Di Vito L, Nazarali S, Gauthier I, Syed M, Chahal J, Ammar M, Carbonelli M, De Negri AM, Sadun A. Differences in onset between eyes in patients with Leber's hereditary optic neuropathy (LHON). Acta Ophthalmologica. 2017 Sep;95.
- 15. Wong A, Cavelier L, Collins-Schramm HE, Seldin MF, McGrogan M, Savontaus ML, Cortopassi GA. Differentiation-specific effects of LHON mutations introduced into neuronal NT2 cells. Human Molecular Genetics. 2002;11(4):431-8.
- 16. Pello R, Martín MA, Carelli V, Nijtmans LG, Achilli A, Pala M, Torroni A, Gomez-Duran A, Ruiz-Pesini E, Martinuzzi A, Smeitink JA. Mitochondrial DNA background modulates the assembly kinetics of OXPHOS complexes in a cellular model of mitochondrial disease. Human Molecular Genetics. 2008;17(24):4001-11.
- 17. Bu XD, Rotter JI. X chromosome-linked and mitochondrial gene control of Leber hereditary optic neuropathy: evidence from segregation analysis for dependence on X chromosome inactivation. Proceedings of the National Academy of Sciences. 1991;88(18):8198-202.
- 18. Giordano C, Montopoli M, Perli E, Orlandi M, Fantin M, Ross-Cisneros FN, Caparrotta L, Martinuzzi A, Ragazzi E, Ghelli A, Sadun AA. Oestrogens ameliorate mitochondrial dysfunction in Leber's hereditary optic neuropathy. Brain. 2010;134(1):220-34
- 19. Nikoskelainen EK, Savontaus ML, Wanne OP, Katila MJ, Nummelin KU. Leber's hereditary optic neuroretinopathy, a maternally inherited

disease: a genealogic study in four pedigrees. Archives of Ophthalmology. 1987;105(5):665-71.

- 20. Newman NJ, Lott MT, Wallace DC. The clinical characteristics of pedigrees of Leber's hereditary optic neuropathy with the 11778 mutation. American Journal of Ophthalmology. 1991;111(6):750-62.
- 21. Johns DR, Smith KH, Miller NR, Sulewski ME, Bias WB. Identical twins who are discordant for Leber's hereditary optic neuropathy. Archives of Ophthalmology. 1993;111(11):1491-4.
- 22. Harding AE, Sweeney MG, Govan GG, Riordan-Eva P. Pedigree analysis in Leber hereditary optic neuropathy families with a pathogenic mtDNA mutation. American Journal of Human Genetics. 1995;57(1):77.
- 23. Biousse V, Brown MD, Newman NJ, Allen JC, Rosenfeld J, Meola G, Wallace DC. De novo 14484 mitochondrial DNA mutation in monozygotic twins discordant for Leber's hereditary optic neuropathy. Neurology. 1997;49(4):1136-8.
- 24. Lam BL. Identical twins no longer discordant for Leber's hereditary optic neuropathy. Archives of Ophthalmology. 1998;116(7):956-7.
- 25. Kirkman MA, Yu-Wai-Man P, Korsten A, Leonhardt M, Dimitriadis K, De Coo IF, Klopstock T, Chinnery PF. Gene–environment interactions in Leber hereditary optic neuropathy. Brain. 2009;132(9):2317-26.
- 26. Barboni P, Savini G, Valentino ML, Montagna P, Cortelli P, De Negri AM, Sadun F, Bianchi S, Longanesi L, Zanini M, de Vivo A. Retinal nerve fiber layer evaluation by optical coherence tomography in Leber's hereditary optic neuropathy. Ophthalmology. 2005;112(1):120-6.
- 27. Savini G, Barboni P, Valentino ML, Montagna P, Cortelli P, De Negri AM, Sadun F, Bianchi S, Longanesi L, Zanini M, Carelli V. Retinal nerve fiber layer evaluation by optical coherence tomography in unaffected carriers with Leber's hereditary optic neuropathy mutations. Ophthalmology. 2005;112(1):127-31.
- 28. Dorfman LJ, Nikoskelainen E, Rosenthal AR, Sogg RL. Visual evoked potentials in Leber's hereditary optic neuropathy. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1977;1(6):565-8.
- 29. Jarc-Vidmar M, Tajnik M, Brecelj J, Fakin A, Sustar M, Naji M, Stirn-Kranjc B, Glavač D, Hawlina M. Clinical and electrophysiology findings in Slovene patients with Leber hereditary optic neuropathy. Documenta Ophthalmologica. 2015 Jun 1;130(3):179-87.
- 30. Guy J, Feuer WJ, Porciatti V, Schiffman J, Abukhalil F, Vandenbroucke R, Rosa PR, Lam BL. Retinal ganglion cell dysfunction in asymptomatic G11778A: Leber hereditary optic neuropathy. Investigative Ophthalmology & Visual Science. 2014;55(2):841-8.
- 31. Viswanathan S, Frishman LJ, Robson JG, Harwerth RS, Smith E3. The photopic negative response of the macaque electroretinogram: reduction by experimental glaucoma. Investigative Ophthalmology & Visual Science. 1999;40(6):1124-36.
- 32. Machida S, Gotoh Y, Tanaka M, Tazawa Y. Predominant loss of the photopic negative response in central retinal artery occlusion. American Journal of Ophthalmology. 2004;137(5):938-40.
- 33. Tamada K, Machida S, Yokoyama D, Kurosaka D. Photopic negative response of full-field and focal macular electroretinograms in patients with optic nerve atrophy. Japanese Journal of Ophthalmology. 2009;53(6):608.
- 34. Kim HD, Park JY, Ohn YH. Clinical applications of photopic negative response (PhNR) for the treatment of glaucoma and diabetic retinopathy. Korean Journal of Ophthalmology. 2010 Apr 1;24(2):89-95.
- 35. Colotto A, Falsini B, Salgarello T, Iarossi G, Galan ME, Scullica L. Photopic negative response of the human ERG: losses associated with glaucomatous damage. Investigative Ophthalmology & Visual Science. 2000;41(8):2205- 11.
- 36. Viswanathan S, Frishman LJ, Robson JG, Walters JW. The photopic negative response of the flash electroretinogram in primary open angle glaucoma. Investigative Ophthalmology & Visual Science. 2001;42(2):514-22.
- 37. Moss HE, Park JC, McAnany JJ. The photopic negative response in idiopathic intracranial hypertension. Investigative Ophthalmology & Visual Science. 2015;56(6):3709-14.
- 38. Kirkiewicz M, Lubiński W, Penkala K. Photopic negative response of full-

RESEARCH

field electroretinography in patients with different stages of glaucomatous optic neuropathy. Documenta Ophthalmologica. 2016;132(1):57-65.

- 39. Peragallo JH, Newman NJ. Is there treatment for Leber hereditary optic neuropathy?. Current Opinion in Ophthalmology. 2015;26(6):450.
- 40. Klopstock T, Yu-Wai-Man P, Dimitriadis K, Rouleau J, Heck S, Bailie M, Atawan A, Chattopadhyay S, Schubert M, Garip A, Kernt M. A randomized placebocontrolled trial of idebenone in Leber's hereditary optic neuropathy. Brain. 2011;134(9):2677-86.
- 41. Klopstock T, Yu-Wai-Man P, Dimitriadis K, Rouleau J, Heck S, Bailie M, Atawan A, Chattopadhyay S, Schubert M, Garip A, Kernt M. A randomized placebocontrolled trial of idebenone in Leber's hereditary optic neuropathy. Brain. 2011;134(9):2677-86.
- 42. Koilkonda RD, Yu H, Chou TH, Feuer WJ, Ruggeri M, Porciatti V, Tse D, Hauswirth WW, Chiodo V, Boye SL, Lewin AS. Safety and effects of the vector for the Leber hereditary optic neuropathy gene therapy clinical trial. JAMA Ophthalmology. 2014;132(4):409-20.
- 43. Marella M, Seo BB, Thomas BB, Matsuno-Yagi A, Yagi T. Successful amelioration of mitochondrial optic neuropathy using the yeast NDI1 gene in a rat animal model. PloS one. 2010;5(7):e11472.
- 44. Carvalho LS, Vandenberghe LH. Promising and delivering gene therapies for vision loss. Vision Research. 2015;111:124-33.