Neuroanatomy, the Achille's heel of medical students. A systematic analysis of educational strategies for the teaching of neuroanatomy.

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Running title: Review on strategies for teaching of neuroanatomy

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ABSTRACT

Neuroanatomy has been deemed crucial for clinical neurosciences. It has been one of the most challenging parts of the anatomical curriculum and is one of the causes of "neurophobia", whose main implication is a negative influence on the choice of neurology in the near future. In the last decades, several educational strategies have been identified to improve the skills of students and to promote a deep learning. The aim of this study was to systematically review the literature to identify the most effective method/s to teach human neuroanatomy. The search was restricted to publications written in English language and to articles describing teaching tools in undergraduate medical courses from January 2006 through December 2017. The primary outcome was the observation of improvement of anatomical knowledge in undergraduate medical students. Secondary outcomes were the amelioration of long-term retention knowledge and the grade of satisfaction of students. Among 18 selected studies, 44.4% have used three-dimensional (3D) teaching tools, 16.6% near peer teaching tool, 5.55% flipped classroom tool, 5.55% applied neuroanatomy elective course, 5.55% equivalence based instruction-rote learning, 5.55% mobile augmented reality, 5.55 % inquiry-based clinical case, 5.55% cadaver dissection, and 5.55% Twitter. The high in-between study heterogeneity was the main issue to identify the most helpful teaching tool to improve neuroanatomical knowledge among medical students. Data from this study suggest that a combination of multiple pedagogical resources seems to be the more advantageous for teaching neuroanatomy.

Keywords: neuroanatomy education, medical education, undergraduate education, neuroscience, teaching; learning; medical students, knowledge retention, students satisfaction,

INTRODUCTION

Anatomy is recognized as one of the disciplines with the longest history in medicine (McLachlan and Patten, 2006; Moxham et al., 2014) and gross anatomy has generally been considered as an essential requirement in the medical curriculum and as a core element for the teaching of biomedical sciences (Drake et al., 2009). Nevertheless, it has been reported that medical courses worldwide have significantly decreased the number of hours devoted to the anatomical sciences (e.g., Drake, 1998, 2002, Deake et al., 2009; Drake, 2014; Moxham and Plaisant, 2007; Moxham and Pais, 2017; McBride and Drake, 2018). Although neuroanatomy is deemed crucial for clinical neurosciences (e.g., Hazelton, 2011), together with physiology and pharmacology being considered relevant for daily clinical practice (e.g., Arráez-Aybar et al., 2010), it has been reported that neurosciences and neuroanatomy have been particularly affected by changes to the medical curriculum (Allen et al., 2016). McBride and Drake (2018) however found that, although within US medical courses between 2002 and 2017 average numbers of contact hours for neuroanatomy only decreased from 95 hours to 80 hours, there has been a major change from 'stand-alone courses to neuroanatomy only appearing in integrated courses. Furthermore, laboratory hours in neuroanatomy have decreased by 38% since 2014.

It is claimed that changes to anatomy teaching have resulted in a 'knowledge decline' in the subject among both undergraduate and graduate students (Waterston and Stewart, 2005) and experienced clinicians are reported to be concerned about the inadequate anatomical knowledge of medical graduates (Waterston and Stewart, 2005; Turney, 2007; Fitzgerald et al., 2008; Johnson et al., 2012). Such sentiments are perhaps confirmed by reports of increased 'error

rates' amongst young doctors and of increased medico-legal litigations for malpractice (Waterston and Stewart, 2005; McHanwell et al., 2007; Estai and Bunt, 2016).

To compound the problem of there being less opportunity to teach anatomy and neuroanatomy, it has been reported that information acquired is easily forgotten by students, even a few months after the end of their courses (e.g., Billings-Gagliardi and Mazor, 2009; Bergman et al., 2011). D'Eon et al. (2006) assessed knowledge loss among medical students attending their second year of studies: while the level of knowledge loss about immunology and physiology was expected, the loss in neuroanatomy knowledge was considerable, probably explained by the perceived complexity of neuroanatomy or poor teaching (Jozefowicz, 1994; Schon et al., 2002; Flanagan et al., 2007; Zinchuk et al., 2010; Hazelton, 2011; Abulaban et al., 2015). The retention of acquired knowledge is also a problem for graduated medical students (Mateen and D'Eon, 2008). Pandey and Zimitat (2007) have stated that efficient learning requires a balance between understanding, observation and memory. Given that laboratory hours in neuroanatomy have declined considerable (McBride and Drake, 2018), it would not be surprising to relate failure to retain neuroanatomical knowledge to the lack of observational experience.

Both the teaching and learning of neurosciences are often considered to be difficult (Jozefowicz, 1994; Abulaban et al., 2015; Arantes et al., 2017). Indeed, neuroanatomy is one of the most challenging parts of the anatomical curriculum and is not infrequently regarded as one of the causes of 'neurophobia' - a fear of the neural sciences; this phobia often relates to the inability to apply neuroscience knowledge to the clinical situation (Jozefowicz, 1994; Schon et al., 2002; Flanagan et al., 2007; Ridsdale et al., 2007; Zinchuk et al., 2010; Hazelton, 2011; Matthias et al.,

2013; Javaid et al., 2018). Perhaps underrecognized, neurophobia seems to be a common condition that affects students at various phases of their medical education (McCarron et al., 2014; Abushouk and Duc, 2016). Its main effect is a negative influence on the choice of neurology as a future career path in medicine (Dall et al., 2013; Abushouk and Duc, 2016). This is unfortunate since, taking into account the ageing population and the global burden of neurological diseases, this represents a public health issue (Menken et al., 2000; Abushouk and Duc, 2016; Arantes et al., 2017).

Although neurophobia has probably multifactorial origins, educational methods and learning strategies based on superficial learning and rote-learning probably have a great influence. These are associated with low interest levels, poor knowledge acquisition and the use by students of strategies just to pass assessments and examinations. This is regrettable since a university education should encourage deep learning approaches that enhance subject interest and leads students to try to more fully understand what they are studying (Giles, 2010; Kam et al., 2013; McColgan et al., 2013; Dao et al., 2015). This issue has been debated in the context of neuroanatomy by Moxham et al. (2015a).

During recent times, several educational strategies have been employed to improve students' skills (Rizzolo et al., 2010). While a core syllabus for neuroanatomy in the medical curriculum has been published (Moxham et al., 2014, 2015a, b), the mode of delivery varies considerable between institutions (Javaid et al., 2018). Since the Renaissance, cadaveric dissection has been considered the 'gold standard' (Biasutto et al., 2006; McLachlan and Patten, 2006; Azer and Eizenberg, 2007; Korf et al., 2008; Moxham et al., 2014). Furthermore, many studies

demonstrate that students prefer dissection, favoring deep learning, providing a three-dimensional perspective of structures (Azer and Eizenberg, 2007; Macchi et al., 2007; Korf et al., 2008; Patel and Moxham, 2006, 2008; Moxham and Moxham, 2007; Moxham and Plaisant, 2007; Kerby et al., 2011; Moxham et al., 2011; Zurada et al., 2011; Olowo-Ofayoku and Moxham, 2014; Estai and Bunt, 2016). It is claimed that dissection is time consuming, requires acquisition of cadavers, involves high costs, and , for formalin, could be associated with health risks (Bay and Ling, 2007; Estai and Bunt, 2016). However, these notions remain debatable (see, for example, Brenner, 2014). Because of perceived obstacles to the dissection, anatomists sometimes have resorted to other resources to improve students' learning of neuroanatomy. Virtual reality (VR) and augmented reality (AR) are some of the latest technologies created in order to overcome the abovementioned obstacles and to provide learning opportunities for students outside the cadaver laboratory. While VR simulates the real environment, in AR the real environment is used as background and a reality is reproduced adding elements of the real word (e.g., sounds, animations, video, etc.) (Billinghurst M, 2002). The developments of mobile technologies have made AR possible via mobile devices. A modern technique of 3D printing system has recently been introduced into anatomy curriculum: 3D printing models can be excellent educational tools, more robust and less toxic than fixed tissue (McMenamin et al., 2014, Lim et al., 2016, Vaccarezza and Papa, 2014, Natfulin JS et al., 2015). Cross-sectional imaging is the starting point from which are developed 3D reconstructions, subsequently used for 3D printing (Javan R et al., 2017; Karakas AB et al., 2018). Applications range from education and training, to assistance in daily surgical practice (Baskaran V et al., 2016) (e.g. the 3D models of brain arteriovenous malformation used as an adjuvant in surgical planning and informed consent to the patients) (Dong M et al., 2018).

The aim of the present study is to review systematically the literature to identify the most effective method(s) of teaching human neuroanatomy, analyzing the studies that explore neuroanatomy teaching tools among undergraduated medical courses and evaluating their impact on improvement of knowledge.

MATERIALS AND METHODS

Search strategy

PubMed (United States National Library of Medicine, Bethesda, MD) and Google Scholar (Google, Inc., Mountain View, CA) bibliographic databases were searched, from January 2006 through to September 2017. Combinations of the following search terms and subheadings were considered appropriate for the present investigation: 'teaching', 'education', 'neuroanatomy', 'learning'.

Inclusion and exclusion criteria

Publications chosen were restricted to those written in English and to articles that described teaching tools/methodologies within undergraduate medical courses. All fields of neuroanatomy (morphology/histology/embryology/fibre tracts) were included in the research.

Studies involving undergraduate dental or healthcare students, graduated medical doctors or residents, retrospective studies, expert reviews and case-reports were excluded. Unpublished sources of data were also excluded as the quality of the work could not be confidently evaluated where there were no peer-review processes. In addition to the electronic searches, bibliographies of retrieved articles and existing systematic reviews that were concerned with teaching tools/methodologies for neuroanatomy were manually searched.

Study selection

The primary interest of this study was related to changes in anatomical knowledge of the undergraduate medical students (i.e. improvement in anatomical structures recognition and/or in understanding of organ relationships). Improvements in long-term retention of knowledge and the levels of student satisfaction were secondary and critical areas of interest. All comparative studies reporting at least one of the primary or the secondary interests were considered suitable for inclusion. Studies not including useful elements for the analysis were excluded in a second round of selection.

The first exclusion step was based on screening of the titles of publications and the second step was based on screening of abstracts. Original articles were then retrieved and full texts were screened for final inclusion and data extraction. Any differences were resolved following discussions between and thus by consensus.

Selected teaching strategies:

- Three-dimensional (3D) models: these instruments allow anatomical structures to be moved in various spatial planes and into different positions. The 3D models may be digital or physical models (e.g., clay models). Digital models display the virtual, or augmented, reality via computer screens (also mobile augmented reality, mAR) or with special stereoscopic displays; "3D technologies" and“3D models”are used in this context as synonyms.

- Flipped classroom teaching (FCT): this is an instructional method in which the students obtain the didactic information before class; the class time then is used to deepen understanding of the newly gained knowledge with peers and teachers;
- Near peer teaching (NPT): this is a tutoring educational model in which senior students or junior doctors act as trainers to more junior students;
- Cadaveric dissection: this involves the dismembering of the human body to study anatomical structures;
- Applied Neuroanatomy Elective (ANE): this is an educational strategy designed with the purpose of increase the understanding of neuroanatomy with a focus on neurosensory pathways, by applying the material to real-world situations through interactive activities and clinical vignettes;
- Twitter: this is an instrument which uses social media as an instrument to increase students' learning and engagement;
- Inquiry-based clinical case (IBCC): this is an educational method aimed at improving the students' critical thinking and content knowledge. Clinical case studies are used during lectures to increase the understanding of neuroanatomy and thus the traditional lecture is transformed into a Socratic debate. The students are required to apply their anatomical knowledge in a broader context;
- Equivalence based instruction (EBI): this is an instructional method that allows students to learn without direct instruction. It is based upon the theory of 'stimulus equivalence'.

Data extraction

A standardized, electronic, *ad hoc* form was designed to enable data extraction. Two reviewers independently analyzed and crosschecked selected articles and extracted data. Discrepancies in the assessment of the articles and data extraction were resolved by a third investigator.

No ethical clearance was required for this study since all selected studies had previously received ethical approval from local institutional review boards.

Study quality assessment

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Moher et al., 2009) were used as a guideline for the present systematic review. The inter-rater agreement obtained for the study selection and data extraction from the included studies was found to be greater than 95% and discrepancies were resolved by consensus.

Statistical analysis

A descriptive analysis of the qualitative variables was carried out employing both absolute and relative (percentage) frequencies. A formal meta-analysis was not performed because of the heterogeneity of the retrieved data.

RESULTS

Selection of the studies

The search through the scientific literature identified 276 citations. Only 18 studies were selected, as summarized in the PRISMA flowchart (Fig. 1). Their characteristics are summarized in Table I.

Characteristics of the selected studies

The total number of participating students was 2,165, with only one study not stating the sample size. More than half the participating students were females (59.6%), even if nine studies (52.9%) did not describe the male:female sex ratio (Macchi et al., 2007; Hall et al., 2013 and 2014; Greenwald and Quitadamo, 2014; Dao et al., 2015; Allen et al., 2016; Greville et al., 2016; Rae et al., 2016; Stephens et al., 2016). Seven (38.8%) out of the 18 studies (Estevez et al., 2010; Chariker et al., 2012; Greenwald and Quitadamo, 2014; Dao et al., 2015; Rae et al., 2016; Goodarzi et al., 2017; Stepan et al., 2017) were conducted in US. Five (27.7%) studies (Hall et al., 2013, 2014; Greville et al., 2016; Hennessy et al., 2016; Stephens et al, 2016) were from the UK. with one study (5.5%) each from the following counties: Germany (Kockro et al., 2015), India (Veeramani et al., 2015), Turkey (Küçük et al., 2016), Columbia (Akle et al., 2018), Canada (Allen et al., 2016) and Italy (Macchi et al., 2007) .

Nine (50%) studies (Macchi et al., 2007; Hall et al., 2014; Kockro et al., 2015; Rae et al., 2016; Allen et al., 2016; Hennessy et al., 2016; Küçük et al., 2016; Stephens et al., 2016; Akle et al., 2018) taught neuroanatomy on courses for second year students. Three (16.6%) studies (Estevez et al., 2010; Dao et al., 2015; Veeramani et al., 2015) taught first year students, with two (11.1%) studies (Greville et al., 2016; Stepan et al., 2017) reported on courses for both first and second year students. Only one (5.5%) study (Hall et al., 2013) reported on a course for third and fourth year students. Three reports (16.6%) (Chariker et al., 2012; Greenwald and Quitadamo, 2014; Goodarzi et al., 2016) did not describe the timing of their neuroanatomy courses.

Selected teaching strategies:

Eight different teaching methodologies were identified in the 18 selected studies: 3D teaching tools, FCT, NPT,cadaveric dissection, ANE,Twitter, IBCC, EBI

Eight (44.4%) studies (Estevez et al., 2010; Chariker et al., 2012; Kockro et al., 2015; Allen et al., 2016; Goodarzi et al., 2017; Küçük et al., 2016; Stepan et al., 2017; Akle et al., 2018) employed **3D teaching tools**. These instruments allow anatomical structures to be moved in various spatial planes and into different positions. The 3D models may be digital or physical models (*e.g.,* clay models). Digital models display the virtual, or augmented, reality via computer screens (also mobile augmented reality, mAR) or with special stereoscopic displays. Three (16.6%) reports (Hall et al., 2013, 2014; Stephens et al., 2016) mentioned near peer teaching (NPT) in which senior students or junior doctors act as trainers to more junior students.

Two (11.1%) studies (Macchi et al., 2007; Rae et al., 2016) reported using cadaveric dissection.

One (5.6%) study (Veeramani et al., 2015) used flipped classroom teaching (FCT) where the students obtained the didactic information before class so that the classroom time permitted the teacher(s) to deepen understanding of the newly acquired knowledge with both student peer and teachers.

One (5.6%) report (Dao et al., 2015) describes an applied neuroanatomy elective (ANE). For this course, there was a focus on neurosensory pathways. The educational strategy employed was designed with the purpose of increasing the understanding of neuroanatomy by applying the

material to real-world situations through interactive activities and clinical vignettes. Being an elective course, student participation was optional.

One (5.6%) study (Hennessy et al., 2016) reported on the use of social media, specifically 'Twitter', as an instrument to increase students' learning and engagement.

One (5.6%) study (Greenwald and Quitadamo, 2014) used inquiry-based clinical cases (IBCC) aimed at improving the students' critical thinking and content knowledge. Clinical case studies are provided during lectures to increase the understanding of neuroanatomy and thus the traditional lecture is transformed into a 'Socratic debate' where the students are required to apply their anatomical knowledge in a broader context. This has correspondences to 'problem-based teaching'.

One (5.6%) study (Greville et al., 2016) employed rote learning equivalence-based instruction (EBI) that is based upon the theory of 'stimulus equivalence' (Sidman, 2008) and that aims to allow students to learn without direct instruction.

Notable for their absence was mention of direct instruction and didactic teaching alone (either in lectures, seminars or small groups), problem-based learning, research-led teaching and learning, reciprocal teaching where cognitive strategies such as summarizing, questioning, clarifying and predicting are emphasized, cooperative versus competitive learning, web-based teaching and learning, use of simulations.

Fourteen (77.7%) studies (Macchi et al., 2007; Estevez et al., 2010; Chariker et al., 2012; Hall et al., 2013, 2014; Greenwald and Quitadamo, 2014; Dao et al., 2015; Veeramani et al., 2015; Allen et al., 2016; Hennessy et al., 2016; Küçük et al., 2016; Rae et al., 2016; Stephens et al., 2016; Akle et al., 2018) achieved primary outcomes, whereas three (16.6%) studies claimed achievement of the secondary outcomes (Kockro et al., 2015; Greville et al., 2016; Stepan et al., 2017). Only one (5.5%) study (Goodarzi et al., 2017) did not show a significant learning improvement.

Primary outcome

Primary outcome was defined as an improvement in recognition of anatomical structures and/or in understanding of organ relationships. Fourteen (77.7%) studies achieved primary outcome. Among 14 studies that met the primary outcome, five (35.7%) used a 3D teaching tool, three (21.4%) a near peer teaching tool, two (14.2%) a cadaver dissection method, one (7.1%) a flipped classroom tool, one (7.1%) the social media ('Twitter') tool, one (7.14%) the IBCC tool and one (7.1%) a ANE course.

Allen et al. (2016) reported on how a 3D neuroanatomy e-learning module could significantly improve the knowledge of the spatial complexity of neuroanatomical structures and of their relationships. Participants were divided into two groups: online 3D learning resources were provided to one group, followed by a cadaveric laboratory session, and vice versa for the other group. All participants completed an identical test pre- and post-teaching to assess anatomy knowledge: both groups scored significantly higher in comparison with the baseline evaluation ($P < 0.01$). In particular, students who initially accessed the 3D online resources scored

significantly better than those who initially were provided with just two-dimensional (2D) resources ($P < 0.01$). Akle et al. (2017) and Estevez et al. (2010) showed the efficacy of 3D clay models in neuroanatomy education. Quiz scores of students that constructed models were significantly higher than those who were taught in a more traditional manner (2D) ($P < 0.05$). Furthermore, the percentage of correct answers on the knowledge quiz was significantly higher in the clay model class ($P < 0.0001$). Chariker et al. (2012) reported on the usefulness of computer-based instruction using 3D computer graphical models. They found that learning anatomy from whole dissections prior to sectional anatomy improved performance by a factor of 1.5 and 10 for easier and more difficult items, respectively. Kücük et al. (2016) found that a group of students who studied anatomy via mobile augmented reality were more successful and had lower cognitive loads than the group who studied without this tool. The authors administered two tests both to experimental and control groups: an academic achievement test (AAT) (30 multiple choices) and cognitive load score (CLS). ANOVAs for AAT and CLS scores were statistically significant in the experimental group.

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Veeramani et al. (2015) investigated the efficacy of the flipped classroom method. Students felt that this method promoted active learning and enhanced their capacity to perform better in their examinations compared with traditional lectures.

Rae et al. (2016) evaluated both short- and long-term knowledge retention of students following brain dissection. They reported that short- and long-term (i.e., after 5 months) retention was significantly better when compared with knowledge assessed before the intervention. The short-term retention was tested immediately after the brain dissection: students' post-test scores were

significantly higher than their pretest scores ($P \leq 0.0001$). Long-term retention was evaluated by conducting an identical assessment five months after completion of the course. Students who participated in the dissection activity had significantly higher scores than those who did not participate in the dissection activity ($P \leq 0.05$).

Macchi et al. (2007) reported on positive experiences from a brief course of dissection, an improvement in neuroanatomical knowledge being found for 57% of students. Furthermore, assessment of long-term knowledge retention showed that the group which had participated in the brief dissection course correctly identified 65% of the structures in a test compared with a 40% recognition within the control group of students who had not participated in the dissection course ($P < 0.05$).

All three studies where near peer teaching was used achieved the primary outcome of improving neuroanatomical knowledge. Hall et al. (2013) reported that there was an increase of perceived level of knowledge, both senior medical students and junior doctors helping to improve the perceived level of knowledge compared with ratings before the sessions. Nevertheless, in a further investigation, Hall et al. (2014) reported that the increased level of knowledge was significantly higher for those who interacted with a senior medical student compared who those who were taught by junior doctors. A similar result was described by Stephens et al. (2016) where medical students from the third and fourth year were rated to be significantly better than medical students from the fifth year or than junior doctors.

Dao et al. (2014) stated that students perceived there to be an improvement in their knowledge after the attending an applied neuroanatomy elective course where neurosensory pathways were related to 'real-world situations' by means of interactive activities and clinical vignettes.

The introduction of a social media tool ('Twitter') to support students' learning on a neuroanatomy module was reported by Hennessey et al. (2016). Spearman's correlation coefficient suggested that there was a small, but statistically significant, relationship between examination scores and viewing frequency ($r_s = 0.189$; $P = 0.04$). No significant difference was however found between examination scores and contribution frequency ($r_s = 0.047$, $P=0.62$). Nevertheless, all students who failed the examination showed a lower frequency of hash tag use.

Secondary outcomes

Secondary outcomes were defined as improvements in long-term retention of knowledge and the levels of student satisfaction. Three (16.6%) studies achieved a secondary outcome. In the study of Kockro et al. (2015), students were exposed to 2D and 3D teaching. The 3D image was created using a stereo-projector system which threw a stereoscopic image on a special screen. Students were asked to wear stereoscopic glasses during the presentation. No differences were found between groups of students who were exposed to 2D and 3D teaching. However, students rated the 3D method superior to 2D teaching in four domains: spatial understanding, application in future anatomy classes, effectiveness, enjoyableness. Similar results were found by Stephan et al. (2016) who used an immersive virtual reality experience. They found that there were no significant differences in anatomy knowledge between students taught with 2D or 3D materials.

However, the 3D group found the learning experience to be significantly more enjoyable and useful and scored significantly higher on the motivation assessment.

Considering that esoteric jargon and technical language within the discipline of neuroanatomy could potentially be responsible for erecting barriers to learning, Greville et al. (2016) evaluated the effectiveness of learning resources for EBI (rote learning equivalence based instruction). They found that the teaching of a small number of direct relationships between stimuli (e.g., anatomical regions, their function, and pathology) resulted in knowledge improvement and the student feedback indicated they had a highly positive learning experience (mostly for the improved confidence and engagement).

DISCUSSION

A variety of educational strategies and approaches for teaching neuroanatomy have been adopted, and investigated, that aim at improving student learning in terms of both short-term and long-term knowledge retention. Drivers for changing strategies and approaches relate primarily to changes in the medical curriculum that have affected all the anatomical sciences, although it is also recognized that retention of neuroanatomical knowledge needs to be enhanced.

Despite purported difficulties with cadaveric dissection (viz. costs, health risks, and ethical-medical issues), this approach remains the 'gold standard', not only in the opinion of anatomists (e.g., Patel and Moxham, 2006, 2008; Johnson et al., 2012) but also according to medical students from different cultural backgrounds who are studying anatomy by means of a variety of educational approaches (Moxham and Moxham, 2007; Moxham and Plaisant, 2007; Kerby et al.,

2011; Zurada A et al., 2011; Olowo-Ofayoku and Moxham, 2014; Pais et al., 2017). However, because of the reduction in hours dedicated to the teaching of the anatomical sciences, few institutions now use dissection to teach neuroanatomy (Drake et al., 2009, 2014; McBride and Drake, 2018). Nevertheless, it is worthy of note that, if dissection is targeted toward those anatomical structures that are deeply located, and hence harder for students to appreciate, then dissection may confer benefits related to knowledge retention (Rae et al., 2016).

These analyses suggest that 3D models provide better results compared with other educational strategies, being more effective for the understanding of the spatial arrangement of neuroanatomical structures and also in terms of increasing student satisfaction. 3D technologies can allow students to explore the whole of the human body by permitting students to select a variety of different views. However, clearly they cannot mimic the tactile sensations experienced during cadaveric dissection. Given that it is often said that Millennials prefer to using state-of-the-art technologies (e.g., Strauss and Howe, 2000; Meriac et al., 2010; Twenge et al., 2014), an unexpected finding that emerged from the literature was that physical models may be more beneficial than 3D virtual models when learning anatomy (Khot et al., 2013; Pawlina and Drake, 2013; Preece et al., 2013). Indeed, the clay models described by Estevez et al. (2010) and Akle et al. (2017) seemed to be particularly successful. Limitations on the use of physical models relate to costs (the price varying according to size and materials, for example) and to the possibility of damage caused during their manipulation by the students (Fredieu et al., 2015). Among physical models, the 3D printing plays an important role: the quality of 3D-printed anatomical models is high and can be used also to improve patient personalized treatment (Garas M et al., 2018; Vaccarezza M, 2018). Its cost is elevated, but lower if compared with those of plastinated models

(McMenamin et al., 2014). Although some limitations mainly related to color (one color), this new tool appears promising. Only a limited number of papers on the use of this technique for teaching the neuroanatomy has been published (Javan R et al., 2017).

In comparison to physical models or traditional educational tools (e.g., books, atlases), e-learning digital tools have many advantages. In particular, they are more accessible through computers, mobile apps and/or interactive work-stations and information may be easily updated or revised (Chenkin et al., 2008; Evgeniou and Loizou, 2012; Ruisoto et al., 2012; Jayakumar et al., 2015). Some online software platform, such as SoftChalk, are demonstrated to be an effective pre-class learning tool (Carr JR, 2016). That physical or digital 3D anatomical models are effective learning instruments may however depend heavily on their ability to display complicated neuroanatomical structures as well as the individual's predisposition to studying and learning neuroanatomy.

Near peer teaching (NPT) also appears to be a usefulness teaching approach, although there needs to be more reports to confirm its effectiveness. It should be emphasized that NPT is different to peer teaching in that, whereas the 'peer teacher' is a tutor of a similar age or similar level of learning as the tutee, the 'near peer teacher' could be a junior doctor or a senior medical student who is two to five years ahead in age and learning experience from the tutee (Lockspeiser et al., 2008; Fredieu et al., 2015). Taking into consideration that students have poor self-awareness of their neuroanatomical knowledge (Hall et al., 2016), NPT could be important for helping students to avoid underestimating their abilities. Accordingly, it can be argued that NPT, by providing students with continuous feedback, could be important for improving students' self-awareness by avoiding underestimating their abilities. We would contend that

better awareness of own neuroanatomical knowledge may also have positive benefits for counteracting neurophobia.

Flipped classroom teaching (FCT) is a strategy that is increasingly being employed and that helps both the teaching of neuroanatomy (Veeramani et al., 2015) and of gross anatomy (Morton and Colbert-Getz, 2017). However, as for NPT, more investigations are needed to confirm this. FCT promotes active learning and enhances the students' capacity to perform better in examinations (Veeramani et al., 2015). By minimizing students' passivity, it is possible to envisage that FCT may be an effective instrument for improving deep knowledge of, and long-term retention of, neuroanatomical concepts.

Greville et al. (2016) claim that the learning of neuroanatomy should be based on equivalence based instruction (EBI) in order to overcome problems related to the use in the discipline of 'esoteric language' (possibly one of the main causes of working memory overload). Undeniably, anatomy is a discipline with its own language with its terminology derived from Latin or classical Greek (Pandey and Zimitat, 2007; Smith et al., 2007; Greville et al., 2016; Stephens and Moxham, 2016, 2018). The efficacy of EBI for the teaching of neuroanatomy was demonstrated by Pytte and Fienup (2012) who reported that, on the basis of the 'stimulus equivalence theory', the trainer can choose what to teach explicitly and what is likely to emerge without direct training.

In line with the characterization of the Millennial generation (e.g., Howe and Strauss, 2000; Meriac et al., 2010; Twenge et al., 2014), consideration must be given to the new generation of

university students, the so-called ‘digital natives’. Such students have grown up with information and communication technologies and these might be embedded within their cognitive processes (Prensky, 2010). It could be argued, therefore, that teaching methods must be appropriate for ‘digital natives’ (DiLullo et al., 2011; Küçük et al., 2016) with augmented, virtual reality technology and social media (e.g., Twitter) being more widely used in neuroanatomy education, if only to increase students motivation. The question remains, however, whether these should be the primary means of delivering courses to medical students or whether they should be adjuncts to other educational approaches. Indeed, modes of delivery of courses might not only affect learning and understanding of course material but could also influence behavior and, in this regard, there is often talk about patients being dissatisfied with the lack of personal contact because of reliance on digital technologies.

Finally, most would agree that, by properly engaging students in the delivery of their courses, the goal of any teaching strategy should be to provide a neuroanatomical knowledge for the training of medical doctors who can competently assess and diagnose neurological patients. In this regard, and perhaps controversially, some might argue that neurology is a discipline more fitted for training after finishing the medical degree. As a corollary to this, it would be a moot point whether too much neuroscience is taught during initial medical training. According to this line of argument, perhaps the prevalence of neuroscientists within anatomy faculties would explain the extent of, and depth of, neuroanatomy courses. As a counterargument, Moxham et al. (2015a, b) and Moxham and Pais (2016, 2017) maintain that medical students are experiencing a university education that is not just instrumentalist and that should take them to the boundaries of knowledge and understanding. As a further counterbalance, it must be acknowledged that there is

a need to develop a core syllabus for neuroanatomy in the medical curriculum. The Anatomical Society in the UK has published a core syllabus for gross anatomy that includes some learning objectives for neuroanatomy (McHanwell et al., 2007; Smith et al., 2016) and the first stages of a more detailed core syllabus specifically for neuroanatomy has been published by the International Federation of Associations of Anatomy (IFAA), (Moxham et al., 2015b). Whether these can focus the attention of medical educators and aid the goal of producing competent medical practitioners requires that innovation is harnessed to commonsense and common purpose.

It would of interest to conjecture whether the articles surveyed are reflecting incremental changes to the teaching of neuroanatomy or whether there is an underlying paradigm-shift. Clearly, neuroanatomy has in the past been built on similar pedagogic principles to the practical, dissection-based, principles employed to teach and learn gross anatomy. That many of the articles surveyed show a distinct movement away from dissection-based pedagogic principles (for a variety of reasons) is indeed suggestive of a paradigm-shift. Equally clearly, paradigm-shifts of this kind may appear attractive because of their novelty or because of 'political', financial or other practical considerations. However, more importantly we need evidence that there are beneficial effects as outlined in our defined primary and secondary outcomes. That 78% of the studies achieved the primary outcome suggests that the paradigm-shift is beneficial.

Limitations of the study

The following five limitations for the present study are recognized:

1. The studies that were utilized in these analyses, and that satisfied the inclusion criteria, were heterogeneous, not only for the teaching tools and approaches reported, but also for their research methodologies in terms of design, sampling, data collection and analysis. Moreover, because some studies employed a 'blended' approach with dissection and other teaching methods, the outcomes reported could potentially have influenced their findings.

2. One of inclusion criteria was that articles must be written in English. It is possible, therefore, that manuscripts not written in English, but with all other inclusion criteria satisfied, were excluded and that these could have a bearing on the gaining and retention of neuroanatomical knowledge and upon student satisfaction. Additionally, one can question whether studies obtained from a single institution in a country is representative of the students' attitudes at national level.

3. There was diversity in the neuroanatomical topics covered within the curricula of the selected studies. This will persist as a limitation until there is more general agreement about a 'core' syllabus.

4. Despite most of reports achieving their objective of improving both student performance and student satisfaction resulting from their neuroanatomy courses, they did not evaluate the long-term impact of their teaching approaches.

5. Not all the studies reported pre- and post-test scores. Consequently, knowledge improvements, together with possible gains in spatial abilities (according to students' perceptions) were not assessed by means of standardized testing. Furthermore, only a few studies recruited a 'control' group.

6. Although it is very important for the critical evaluation of the results, it was not possible to understand, because not detailed in the selected manuscripts, if other courses, such as physiology, were simultaneously carried out.

CONCLUSIONS

The question concerning the most effective method of teaching neuroanatomy remains unresolved and consequently it is not currently possible to identify a specific teaching tool or approach that can significantly improve the knowledge of neuroanatomy among medical students. Although cadaveric dissection is still regarded as the 'gold standard', other approaches (such as physical and 3D digital modeling) are also effective. In all probability, however, a combination of pedagogical tools and approaches (blended strategies) might be best for teaching neuroanatomy.

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