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Unravelling early endovascular skill acquisition

Paul, Katja

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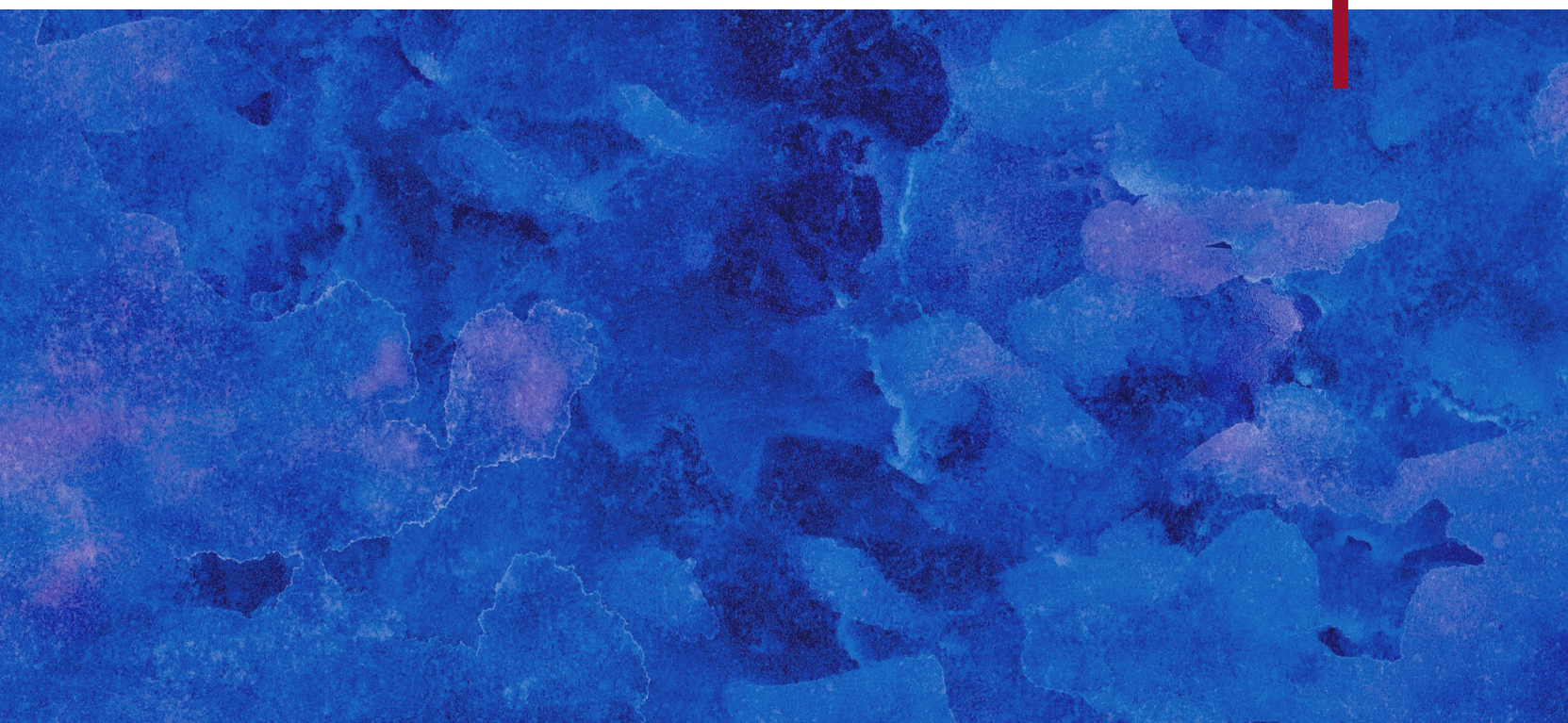
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Introduction

CHAPTER 1



Endovascular interventions (EIs) are minimally invasive procedures to treat vascular disease. In contrast to open surgery, in EIs operators use a small access to an artery or vein and perform the procedures on distant target sites using different types of instrumentation specifically designed for intravascular use. Thus, while vascular surgeons who perform open access procedures can directly see and control the situs by visual and manual means, endovascular operators depend on imaging and remote guidance of instrumentation. Given the shortcomings of all imaging modalities and the limited mechanical control of the instrumentation, mastery of EIs requires numerous cognitive skills not necessarily needed for open surgery. Although nearly half a century has passed since the introduction of EIs into clinical practice, little is known about the specific sub-skills required to learn and to perform EIs safely and effectively. Further, the technology of the instrumentation used for such interventions is rapidly evolving, resulting in increasingly complex techniques. While initially only highly selected patient populations were treated using endovascular technique, now far sicker patients and far more complex disease scenarios are being accepted for treatment (Lanzer 2013). This development is partly caused by the expanding aging population. Thus, due to demographic changes in the population and rapid progress in catheter technology, the need for adequate EI training has increased significantly.

Traditionally, EIs are taught according to the mentor-traineeship model which means that residents first observe and later on assist a senior operator. Once basic skills have been acquired, resident and senior operator switch places meaning that the trainee performs simple EIs assisted by their mentor, followed by the trainee taking over and the mentor standing by. At the final stage, the trainee performs the procedure by him- or herself. Although time-tested, the success of this teaching model depends on a large number of factors. For example, judgments and decision-making are not always verbalized, not all senior operators are skilled communicators and not all trainees are skilled observers. Thus, training is largely implicit and deliberate practice and continuous, structured feedback are frequently missing. Moreover, the mentor-traineeship model lacks reproducible standards and training success varies. Furthermore, training according to the mentor-traineeship model is slow and requires extensive one-on-one sessions (Babineau et al. 2004; Lanzer 2013; Lanzer and Taatgen 2013). Importantly, this teaching technique may also have negative consequences for the patient as they may be exposed to a greater procedural risk if the EI is performed by an inexperienced operator (Lin et al. 2005; Vickers et al. 2009). Thus, to develop explicit endovascular training protocols, deeper insight into core sub-skills that are required to perform EIs safely, is needed. To assure a consistent high-level of procedural expertise, crucial cognitive skills and factors influencing skill acquisition and performance outcomes need to be identified, taken

into account and deliberately practiced.

In this thesis, we set out to determine whether early angiographic skills can be learned based on explicit, standardized training such as written descriptions of procedural steps, instruction videos and limited practice, and to establish whether skill acquisition is influenced by individual differences, such as cognitive ability and manual dexterity. Crucially, in addition to studying behaviour, we aimed to gain insight into plastic brain changes accompanying skill acquisition. Thus, we studied angiographic skill acquisition using a multifaceted approach: on a behavioural level we employed a battery of standardized psychometric tests and multiple means of performance evaluations, to identify plastic brain changes we used multimodal magnetic resonance imaging (MRI). In this thesis, we defined early endovascular skill acquisition as entry-level technical skills needed to perform a carotid artery angiography where the endovascular tools to be used have been predefined. That is, we focused on the psychomotor skills that are necessary to cannulate the arteries, not on higher-level skills such as decision-making.

1.1 Factors complicating performing endovascular interventions

Before explaining the research questions and methods used in greater detail, let us first elucidate what makes endovascular procedures special and what complicates acquiring the necessary skills and performing these procedures successfully.

The fact that EIs are minimally invasive procedures implies that they are performed using a small access site, typically 1.5 to 6 mm in diameter, without direct access to the target situs. Using this access site, operators use high-tech finely tuned instrumentation to reach distant targets. Depending on the patient's body size and vascular territory to be treated, typical distances range on average from 80 to 120 centimetres. Typical access sites are the common femoral artery at the groin level, the radial artery at the wrist level and the brachial artery above the elbow. Following needle puncture of the vessels, a guidewire is inserted through the needle, the needle is withdrawn and replaced by a sheath that secures the access to the vessel. Via this access site, EIs are performed using different tools such as catheters, guidewires, guiding catheters, stents, artificial valves and other devices that are steered towards the target sites where the treatment is performed. Understanding the mechanical properties of the individual instruments, their behaviour within the vascular system and extremely diligent instrument handling are critical for procedural success and patient safety. Due to the multitude of properties of the instruments that influence

their behaviour in the blood vessels and their often small but important differences that need to be taken into account, cognitive and psychomotor skills are essential to master EIs.

To observe the progress of the instrumentation, interventional actions and their results, the operator must rely on images and their interpretation. Classically, x-ray images are used for guidance. More recently, ultrasound and optical coherence tomography images may be used additionally. Fluoroscopy images (dynamic x-ray images) however only provide a limited greyish 2D picture of the target site (Lanzer 2013). This means that the operator has to create a 3D representation of the patient's vascular system mentally to allow proper steering and manipulation of the instrumentation. Frequently, multiple projections are needed to resolve ambiguities. In addition, in moving targets, such as heart, the dynamic components of anatomical changes must be taken into account as well. Another factor complicating image interpretation is the fact that blood vessels are only visible on x-ray images using contrast agent. However, only the lumen of the vessel is visualized, vessel walls must be judged by the contours of the lumen. While multiple projections where appropriate may be beneficial, the amount of contrast agent must be kept as low as possible to protect the kidneys responsible for contrast agent elimination. Furthermore, with increasing length of an EI also the associated risk and radiation exposure to the patient and staff increase. Therefore, the length of an intervention should be kept at a minimum.

From the above follows that to perform a simple, predefined EI operators need to be able to read the fluoroscopy images, create a mental 3D representation of the vascular system and target site, and manipulate the EI instrumentation in 3D space. Thus, the operator needs to learn the fine-grained psychomotor coordination that is necessary to manoeuvre the tools safely and efficiently through the vascular system using this mental representation and visual feedback from the fluoroscopy screen as guidance. Taken together, the factors described above pose extensive visuo-motor demands on trainees learning and performing EIs. In contrast to open surgery, minimally invasive procedures have been associated with a slower learning curve, possibly caused by visuo-motor challenges associated with these procedures (Vickers et al. 2009).

1.2 Deliberate practice and simulator training in minimally invasive procedures

To overcome visuo-motor challenges associated with endovascular procedures, sufficient training and practice are crucial (Lanzer 2013). That is, a high level of

experience has been associated with better patient outcomes in minimally invasive procedures. For example, the risk of cancer re-occurrence after minimally invasive removal of the affected tissue decreased by almost 50 % when operators had performed more than 750 procedures compared to 10 and 250 procedures (Vickers et al., 2009). However, according to Ericsson (2007) not any form of practice, but deliberate practice is necessary to promote skill acquisition and to lead to advanced - and eventually - expert performance. Deliberate practice is defined as dedicated practice, where specific, especially unmastered parts of a skill are trained, and performance is monitored and corrected based on feedback. The current teaching curricula mainly based on the mentor-traineeship model however do not necessarily conform to deliberate practice. This is due to the fact that practice takes largely place on an actual patient, which means that time to explicitly explain is limited and repeatedly practising specific parts of a procedure is virtually impossible. A platform where deliberate practice of early, fundamental endovascular skills can take place safely is in the context of simulator training sessions (Sadideen and Kneebone 2012).

Over the last two decades, simulation as an educational training tool in health care has received increasing attention. Inspired by aviation, and first transferred to laparoscopic surgery, some studies have also revealed promising results in the context of endovascular skill acquisition (Chaer et al. 2006; Dawson et al. 2007; Saratzis et al. 2017; Van Herzele et al. 2010). For example, first-year vascular surgery residents who took part in a two-day simulation training program in which endovascular diagnosis and interventions were practised greatly improved on multiple performance metrics (Dawson et al. 2007). A four-day simulator training course also improved relevant technical skills of vascular surgery residents needed to perform aneurysm repair endovascularly (Saratzis et al. 2017). Technical skills were measured by the simulator as well as by seniors who used subjective Likert scale ratings to assess the quality of procedural steps. In both studies, dedicated one-on-one training was given by a senior who showed the resident how to perform the procedure and provided detailed feedback. The nature of both studies' simulator training protocols might explain why they led to improved technical skills. In both studies, trainees trained according to the principles of deliberate practice. That is, one-on-one training was given and trainees received personalised feedback from an expert, who identified weak parts that were then focused on. Further, in the simulation environment trainees were allowed to make mistakes, observe their consequences, and opportunities for discussion were given to facilitate interactive problem-solving. Thus, simulator training can be a great platform to provide structured training of technical skills to novice and beginning operators.

1.3 Feedback and skill acquisition

To advance psychomotor skill acquisition and performance in minimally invasive procedures, feedback is crucial (Ericsson 2011; Issenberg et al. 2005). Feedback can either be intrinsic or extrinsic. The former is a result that is triggered directly by an action, such as not being able to cannulate an artery with a wrongly chosen catheter (Johnson et al. 2013). The latter, extrinsic feedback, is delivered on top of intrinsic feedback, for example by a mentor who corrects the trainee's actions. In the motor learning literature, the effect of *knowledge of results* (KR) on motor performance and retention is often studied as it can be manipulated more easily than intrinsic feedback. *Knowledge of results* is a specific type of extrinsic feedback that is provided in experiments designed such that KR is the only means to gain insight into task outcomes. *Knowledge of results* provides information about the movement outcome, such as time taken to perform a procedure, or the path length of the tools i.e. metrics often provided by medical simulators (O'Connor et al. 2008). *Knowledge of results* has been shown to improve motor performance and learning, however there are many hypotheses about the mechanism underlying this effect. Plausible, not mutually exclusive hypotheses discussed in a review paper (Salmoni et al. 1984) state that KR leads to the development of schemas of the task and acts as guidance. Schemas are made up of rules that tie motor commands and sensory features to KR. With varied task practice, stronger, more flexible schemas can be developed. Further, KR may have a guidance role by informing the trainee about mistakes that are made and allowing the trainee to recalibrate movements making them increasingly precise (Schmidt et al. 1989). However, if too much guidance is provided, the trainee's performance can become contingent on it, degrading task performance once it is taken away. Asking participants to self-assess their performance outcome before receiving KR may be a way to ease this contingency. In line with these hypotheses, Boyle et al. (2010) showed that a combination of self-assessment, with an expert highlighting errors and showing how to correct them was found to lead to fewer errors in simulator-based laparoscopy procedures compared to no feedback. Thus, through these types of feedback, residents were encouraged to focus attention on aspects of their own task performance, but were also directed towards mistakes they might not have noticed themselves. This may have allowed them to adapt response associations before incorrect responses manifest themselves and may have increased the accuracy of their schemas.

The negative effect of too much feedback on performance was shown by Stefanidis et al. (2007). They found that limited feedback and frequent viewing of a video tutorial led to faster skill acquisition in minimally invasive procedures compared to extensive feedback and singular watching of a video tutorial. Infrequent feedback

might be superior to intense feedback as it leaves room for the trainee to process and develop his or her own strategies to approach the task (Johnson 2013). Further, if feedback is provided at a high frequency, the trainee may not develop insight into his or her own task performance (Schmidt et al. 1989). Being able to view a video tutorial multiple times during a training session may have strengthened the cognitive representation of the task and may have facilitated insight into the technique. However, how much feedback is too much and which types of feedback may be especially beneficial for skill acquisition depends on the task and further research is needed to better understand the relationship between different types of feedback and task types (Stefanidis et al. 2007; Wulf et al. 2010).

The effect of implicit feedback on skill acquisition is much harder to study than explicit feedback as it is inherent to a task and thus cannot be easily manipulated (Salmoni et al. 1984). Therefore, to the best of my knowledge, only very few studies have tested the effect of implicit feedback on simulator-based skills acquisition in health care. An example is a study (Zhou et al. 2012) that compared the effect of haptic feedback to no haptic on simulator-based laparoscopic skill acquisition and found that haptic feedback led to faster skill acquisition. However, the facilitatory effect of haptic feedback was only observable during initial learning. Later on, reliance on visual feedback became more important to learn the required visuo-motor coordination.

In general, it seems reasonable to assume that implicit feedback, such as visual feedback on the movements of the endovascular tools provided by the fluoroscopy screen is vital to endovascular skill acquisition. However, studying its effect on endovascular skill acquisition seems to be of less importance as implicit feedback is already inherent to endovascular procedures. Further, studying implicit feedback would rather yield insights that could be used to improve the technology and usability of endovascular tools, fluoroscopy displays and simulators, not training and is thus out of the scope of this thesis. What can be improved by training is the ability of a trainee to interpret implicit feedback, for example by a mentor who guides the trainee in interpreting fluoroscopy images explicitly. Finally, another function of feedback is stimulating the learners' motivation. That is, if especially positive aspects of task performance are highlighted, feedback can facilitate learning by increasing the trainees' motivation to practice. Interestingly, positive feedback stating that one performs better than average was even found to have a beneficial effect on motor learning if in fact it was not true (Wulf et al., 2010). To summarise, feedback is essential to skill acquisition in minimally invasive procedures, however, care should be taken to the frequency with which it is provided, its content and the timing of delivery (Bosse et al., 2015; Johnson, 2013).

1.4 Upgrading the mentor-traineeship model

An extension of the traditional mentor-traineeship approach to teaching is Peyton's four-step approach which has been applied to and studied in many medical domains. A systematic meta-analysis of randomised-controlled studies that compared Peyton's four-step approach to the standard mentor-traineeship model found that Peyton's four-step approach led to faster skill acquisition and better skill retention (Giacomino et al. 2020). Peyton's four step approach is made up of the following four steps: demonstration, deconstruction, comprehension and performance. These steps comprise a demonstration of the procedure by the teacher, a decomposition into its sub-parts, a demonstration by the teacher based on instructions delivered by the trainee and finally the performance by the trainee him/herself (Walker and Peyton 1998). The comprehension step has been shown to be critical to its success by a study that compared the effectiveness of this teaching method while systematically eliminating steps (Krautter et al. 2015). The significance of the comprehension step might be that it requires motor imagery and actively engages the trainee into the learning process by requiring him or her to think about the sub-components of the task and to provide feedback on the teacher's performance instead of only passively viewing a demonstration. This helps building up a mental model of the required steps and fosters memory recall instead of only recollection (Rossettini et al. 2017). The fourth step is crucial as it involves the teacher providing feedback on the trainee's performance. However, for Peyton's-four step approach to be effective it seems to be crucial that it is applied by an expert performer, not a fellow trainee. Peyton's four-step approach and its success in advancing skill acquisition provide ideas for how skills training could be structured and highlight crucial teaching strategies.

1.5 Individual difference factors that influence skill acquisition

In addition to feedback and teaching strategies, research has shown that pre-existing psychomotor ability may influence the rate of skill acquisition in minimally invasive surgery and Els, especially in novice and beginning operators (Saratzis et al. 2017; Stefanidis et al. 2006; Van Herzeele et al. 2010). Due to the visuo-motor challenges that the trainee is faced with when learning to perform a minimally invasive procedure, tests that measure visuo-spatial or motor skills have often been used to explore the relationship between aptitude and skill acquisition (Langlois et al. 2015). For example, van Herzeele et al. (2010) showed that participants who

performed well on a test measuring visuo-spatial memory used less fluoroscopy during simulated interventions, their technical skills were rated higher as well. Further, higher scores on a manual dexterity test were associated with high initial performance. However, studies linking psychomotor ability to minimally invasive skill acquisition do not always reveal results in line with each other (e.g. Stefanidis et al. 2006; Walker et al. 2019), thus pointing to the need for further research. Nevertheless, such findings suggest that individual differences in psychomotor ability before training influence training success. Thus, testing for psychomotor abilities may allow developing and providing individualised training programs that focus on the aspects that limit the trainee's performance. Hence, it would facilitate using the principles of deliberate practice when developing structured training curricula.

1.6 Brain plasticity and skill acquisition

While behavioural research methods can identify psychometric performance predictors and provide insight into behavioural change, non-invasive imaging methods such as magnetic resonance imaging (MRI) can uncover cortical and subcortical substrates involved in the process of skill acquisition. Over the past several decades, multiple MR imaging methods have been used and further developed to study how the brain adapts as a result of skill acquisition. Widely used techniques include task-based functional MRI (fMRI) measuring the blood oxygen level dependent (BOLD) response associated with performing a task, voxel-based morphometry (VBM) measuring grey matter volume plasticity, diffusion tensor imaging (DTI) assessing change in white matter microstructure, and resting-state fMRI (rs-fMRI), which can provide insight into experience-dependent changes in functional connectivity between brain areas. These techniques can shed light onto which brain areas are crucial to skill acquisition and show where structural and functional changes occur at different learning stages. Further, these methods allow studying individual differences in brain tissue structure/function and linking these to skill acquisition and performance differences. These insights may then further advance developing teaching curricula by informing about the core sub-skills, training schedules and types of training that may be needed (Chang, 2014). The MR imaging techniques listed above are explained briefly in the text box below.

Overview of the used magnetic resonance imaging methods

Non-invasive MRI can be used to quantify training-related changes in micro- and macroscopic brain structure, functional activation and plasticity in functional networks. However, these MRI techniques do not directly measure these properties, but are based on surrogate measures that exploit physiological mechanisms and their different magnetic properties, such as blood oxygen level dependent (BOLD) in fMRI as a measure of brain activity or the direction of water diffusion as a measure of white matter microstructure in diffusion-weighted MRI. Therefore, these methods cannot give any direct insight into the actual neuronal or cellular changes that may have happened (Lerch et al. 2017). Nevertheless, MRI equipped to combine structural-morphologic and topographic information along with parameters of functional activity allows to study plastic changes in the human brain non-invasively. The principles of the three techniques that were used in this thesis as well as task-based fMRI, since this method was used in many of the described studies, are explained below.

Task-based functional magnetic resonance imaging

In task-based fMRI, participants perform a task in the scanner while changes in regional brain activity are measured by computing BOLD signal. BOLD signal is used as a measure of localised brain activity and is based on the fact that increased brain activity leads to an increase in local cerebral blood flow which overcompensates the increased consumption of oxygen resulting in a local increase in oxygenated haemoglobin (oxy-Hb) and a decrease in deoxygenated haemoglobin (deoxy-Hb). As deoxy-Hb is paramagnetic and oxy-Hb is diamagnetic, BOLD signal is mainly determined by the local concentration change of deoxy-Hb. Changes in the concentration of deoxy-Hb inversely relate to BOLD signal and therefore, the drop in deoxy-Hb with increased brain activity leads to a BOLD signal increase (Kwong et al. 1992; Ogawa et al. 1990, 1992). To quantify BOLD signal related to performing a task, a control condition is needed to contrast BOLD signal with and attribute changes in brain activity to the specific task. To calculate BOLD signal from a functional image, multiple pre-processing steps have to be performed after which BOLD signal can be averaged over time and events and statistically compared across conditions.

Voxel-based morphometry

Changes in the grey matter macrostructure in humans based on MR images are typically quantified using voxel-based morphometry (VBM) (Ashburner and Friston 2000). A voxel is a three-dimensional pixel of specified size used to localise and quantify the amount of change in 3D space. In voxel-based

morphometry, a T1-weighted MR images is first segmented into grey matter, white matter and cerebrospinal fluid and bias corrected. Further, the grey matter image is converted to a standard template (spatial normalisation), while keeping track of how each voxel needed to be modulated in order to fit this template. Preserving this information is crucial as one would otherwise lose the information about the morphometry of the individual's brain structure that is of interest in VBM. Spatial normalisation allows comparison across individuals. Each voxel is then multiplied with the modulation parameter to reflect the individual's voxel-wise grey matter volume concentration (Gaser et al. 2022). After smoothing, which increases the signal-to-noise ratio (at the expense of the spatial resolution), voxel-wise maps of grey matter volume can be statistically compared within or/and across individuals (Lerch et al. 2017).

Diffusion-tensor imaging

Diffusion imaging is often used to infer changes in white matter microstructure. Diffusion imaging measures the diffusion of water molecules in tissue and in data analysis, water diffusion is often modelled as a tensor (Diffusion-tensor imaging, DTI, Basser et al. 1994). Changes in the white matter microstructure alter the mobility of water molecules and thus diffusion imaging can provide indirect measures of changes in white matter microstructure (Lerch et al. 2017). Multiple diffusion parameters can be derived using DTI, each capturing different properties of the diffusion pattern. The most commonly used diffusion metric is fractional anisotropy (FA) which assesses the directional deviation of water diffusion from free (isotropic) diffusion (Zatorre et al. 2012). After pre-processing, (smoothed) voxel-wise FA maps can be calculated and statistically compared, e.g., across time, groups, and/or individuals.

Resting-state functional magnetic resonance imaging

Research has shown that even when not engaged in a specific task, low frequency BOLD fluctuations in the brain are temporally and spatially organised (Biswal et al. 1995). That is, even at rest they form functionally organised networks, such as the sensory-motor network or the default mode network which parallel the organisation of anatomical networks (Guerra-Carrillo et al. 2014). The strength of these functional connections in the brain can be influenced by prior behaviour, such as motor training before a rs-fMRI scan and has been attributed to behavioural change (Albert et al. 2009; Ma et al. 2011; Taubert et al. 2010). Methodologically, rs-fMRI measures the temporal correlation in BOLD signal between grey matter voxels in the brain. There are many different metrics that can be calculated based on a rs-fMRI scan to infer functional connectivity and each of these metrics computes connectivity in

a slightly different way. In this thesis, we used intrinsic connectivity contrast (Martuzzi et al. 2011) which calculates the strength of the average absolute correlation between every grey matter voxel of the brain. Before this metric can be calculated, images need to be pre-processed. If for example a before and after learning image was acquired, these images can be statistically compared for voxel-wise change in intrinsic connectivity. made explicit during training.

1.7 Studying skill acquisition using magnetic resonance imaging

Research has shown that the acquisition of motor skills takes place in stages (Dayan and Cohen 2011; Fitts and Posner 1967). Initially, learning will rapidly progress followed by a period where improvements occur more slowly. The actual length of both stages depends on the complexity of the task being practised. On a functional level, these stages are accompanied by changes in brain activity that vary across recruited networks and have been distilled by a review about neuroplasticity related to motor learning (Dayan and Cohen 2011). Fast, initial learning has been linked to increased activation in the pre-motor cortex, supplementary motor area (SMA), parietal cortex, striatum and the cerebellum, while decreased activation in the primary motor cortex (M1), dorsolateral prefrontal cortex (DLPFC), and pre-supplementary motor area (pre-SMA) has been found as a function of rapid skill improvement. Increased BOLD signal has been interpreted as a need for further resources, while decreasing BOLD activity may mean that learning led to more selective synaptic activity implying that processing became more efficient as fewer resources are needed to carry out the task (Poldrack 2000). Furthermore, slow learning has been linked to increased BOLD signal in the SMA, dorsolateral striatum, M1 and the primary somatosensory cortex (S1) and a decrease in cerebellar activity. The spatial reorganisation of brain activity may be related to a decreasing need of executive functioning/cognitive control as task performance approaches automaticity (Dayan and Cohen 2011; Poldrack 2000). Regarding the function of the involved brain regions, a distinction between regions involved in learning of motor and spatial aspects of a task has been suggested by Hikosaka et al. (2002). A fronto-parietal-associative-striatum-cerebellar loop may subserve learning spatial coordinates, while an M1-sensorimotor- striatum-cerebellar circuit may be responsible for the acquisition of motor coordinates. The connections (pre-SMA, SMA and premotor) from the association- to motor cortices are thought to

compute the transformation from spatial to motor coordinates (Dayan and Cohen 2011; Hikosaka et al. 2002). Not only does the pattern of brain activity change as motor learning progresses, but even neural networks active during mental preparation of performing a motor skill have been shown to differ between novices and experts and can be used to distinguish them. A study (Milton et al. 2007) comparing brain activity between expert and novice golfers who imagined the motor sequence of preparing to hit a golf ball found remarkable differences between groups. Only in novices, motor imagery led to activation in the basal ganglia and the limbic system. The authors attributed activation in these regions to mental effort and difficulties in filtering out irrelevant information. In contrast, experts may automatically focus on the crucial sensory information. Compared to novices, experts showed increased BOLD signal in the premotor cortex, superior parietal lobule and occipital areas during motor imagery, possibly related to a global attentional focus. In general, experts activated a smaller volume of the brain while mentally preparing to hit the golf ball than novices. Hence, neural networks activated while planning the motor sequence and performing the necessary visuo-motor transformations are more efficiently organised in expert golfers than in novices. Since mental preparation affects actual golf performance, and differences in activated brain regions between groups point to processing differences, the authors wondered whether teaching how to efficiently filter out irrelevant information during golf training would facilitate learning in golf novices. Thus, this study provides an example of how evidence from neuroimaging studies can give unique insight into processes underlying skilled behaviour and specific strategies that enhance task performance that could be

1.8 Structural and functional brain changes associated with skill acquisition

On a structural level, skill acquisition has also been associated with plastic brain changes. Since the seminal work by Amunts et al. (1997) who found size differences in the hand area of the primary motor cortex between musicians and controls, a large body of research (see Chang, 2014 for a review) has shown that the micro and macroscopic brain structure of experts differs from that of novices in regions related to their specific skill. For example, expert mountain climbers compared to controls had higher grey matter volume (GMV) in lobule I-V of the cerebellum and right posterior parietal cortex. These regions are related to visuo-motor coordination and fine motor control which are crucial to safe practice in mountain climbing (Di Paola et al. 2013). However, results of cross-sectional studies cannot be used to infer causality from these differences. Only brain changes revealed by controlled training studies

can be attributed to skill acquisition directly (Thomas and Baker 2013). A sequence of studies (Draganski et al. 2004; Sampaio-Baptista et al. 2014; Scholz et al. 2009) using the visuo-motor paradigm juggling found evidence of structural plasticity due to long-term training. Draganski et al. (2004) found increased GMV in the intraparietal sulcus and MT/V5 which have been implicated in visuo-motor coordination and motion perception, thus sub-skills that are crucial to juggling. Increases in white matter microstructure -indirectly measured by fractional anisotropy- underlying the region where GMV changes were detected, were also found as a result of juggling training (Scholz et al. 2009). Thus, visuo-motor skill acquisition led to structural grey and white matter plasticity in neighbouring, task-relevant regions. Changes in GMV and in the DTI derived parameters mean diffusivity and fractional anisotropy due to fast learning e.g., one practice session, have also been documented (Irmén et al. 2020; Sagi et al. 2012; Taubert et al. 2016). Rs-fMRI can provide a window into the functional organisation of the brain and reorganisation due to skill acquisition (Guerra-Carrillo et al. 2014). A study conducted by Ma et al. (2011) gives insight into dynamic changes in resting-state functional connectivity (rs-FC) as motor skill acquisition progresses. They showed that during the first two weeks of training a finger tapping sequence in which participants reached asymptotic performance, rs-FC increased in the right postcentral -and supramarginal gyrus. In the following two training weeks, the strength of these rs-FC networks decreased again, however rs-FC in the left supramarginal gyrus continued to increase across all four training weeks. The authors regard this shift in rs-FC in the right postcentral -and supramarginal gyrus as evidence for a decreasing need of sensori-motor integration and visuo-spatial attention as learning progresses. The initial increase in rs-FC may indicate that the right postcentral -and supramarginal gyrus promote early learning via mechanisms such as offline-processing and memory consolidation, while the left supra-marginal gyrus may modulate long-term learning via skill retention. Together, these different neuroimaging methods can provide insight into the time-course, dynamics and behavioural relevance of plastic changes co-occurring with skill acquisition. These in turn may inform the development of training curricula of a specific skill. As of yet however, no study has examined structural and functional brain plasticity as a result of endovascular skill acquisition.

1.9 Studying endovascular skill acquisition

In the present thesis, we have used behavioural and MRI based approaches to gain comprehensive insight into early endovascular skill acquisition and predictors of performance. On a behavioural level, our goal was to determine predictors of learning using cognitive and psychomotor tests, and gain insight into common

mistakes and difficult aspects of the procedure. Further, we explored different methods of performance evaluation. On the brain level, we investigated structural and functional changes as a result of learning and predictors of learning using structural and functional MRI metrics. The methodological approach and research aims are explained in the next sections.

- To examine whether novice operators can acquire endovascular skills during a brief, structured simulator training
- To identify predictors of learning using cognitive and manual dexterity tests
- To investigate whether overall learning of EIs is associated with structural and functional brain change and whether possible changes are behaviourally relevant
- To identify predictors of learning using structural and functional baseline (before learning) MRI parameters

1.10 Methodological approach and overview of this thesis

The first step of this research project was a general literature review into complex skill acquisition and brain plasticity quantified using multimodal MR imaging. Chapter 2 gives a summary and integration of the main findings. The next step was to develop a longitudinal training study, including a training protocol. In this training study, participants first performed cognitive and manual dexterity tests, followed by completing a simulator-based training on an endovascular simulator. Before and after simulator training, we acquired multimodal MR images. To study skill acquisition in a controlled way, we chose to use medical students as participants since they were all equally naïve to the procedure. Residents would have had differing levels of experience in endovascular technique and possibly experience with other surgical procedures confounding EI skill acquisition. Since simulator training is such a promising tool to teach technical skills and the simulator environment allows controlling the patient cases and environmental factors without putting patients at risk, we trained participants on an endovascular simulator. While designing the endovascular training, we took the principles of deliberate practice into account. To be able to attribute structural and functional changes directly to endovascular skill acquisition, we used a separate control group. Keeping all other factors equal, only the training on the simulator differed between groups. Control participants only practised the very first part of the EI that participants in the experimental group learned to perform. To assure that the control group did not practice this part of the procedure many more times than the experimental group after finishing

their respective task, the control group watched screen captures of the rest of the procedure that the experimental group actually learned. On the behavioural level, we wanted to determine whether participants can acquire endovascular skills within a limited time frame and whether results from cognitive and manual dexterity tests would predict the rate of endovascular skill acquisition. To test for behavioural improvements and predictors thereof, we used linear mixed-effect modelling. In Chapter 3, the analysis and answers to these questions are provided. On the brain level, we examined whether endovascular skill acquisition is associated with structural and functional brain plasticity and whether before learning imaging parameters can predict overall performance. To study structural and functional changes due to endovascular skill acquisition we used VBM, DTI and rs- fMRI. Our main focus was to test whether endovascular training had a differential effect on plasticity. Here, we utilised group (experimental vs control group) by time (pre vs post-trainings) interaction analyses with the metrics derived from VBM, DTI and rs-fMRI. To test whether potential brain changes were behaviourally relevant, we correlated changes in the respective metrics with behavioural improvements. Finally, we correlated VBM, DTI and rs-fMRI parameters before learning with training success to determine whether these parameters could predict overall training outcome. The results of these analyses are described in Chapter 4. Chapter 5 provides a general discussion of the main findings. Further, we discuss methodological difficulties, limitations, practical implications of the results for medical education and directions for future research.