



## PhD thesis

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# The Impact of Feedback in Rehabilitation using Advanced Computer-based Technology



“As the ball hit the net, the weakest threads gave way with a sudden snap leaving frayed ends dangling. What previously had been a beautiful structure was now weakened and fragile, unable to function as before.” (*Inge Wilms, 2011*)

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## Preface

This Ph.D. thesis represents a major milestone in my career as a scientist and researcher. Little did I know that the decision eight years ago to enter college, to improve my knowledge in human-computer interaction, would result in a career as a scientist in computer-based cognitive rehabilitation.

During this Ph.D. project, I have had the opportunity to study the effects of intensity, feedback and the progression of level of difficulty in computer-based rehabilitation training in the fields of aphasia and neglect. The neglect studies have been included in this final Ph.D. thesis. The aphasia studies, nevertheless, served to teach me, the hard way, about research in general and the difficulties of rehabilitation research in particular.

The research has provided me with growing of insight into of how wonderfully strange the inner workings of the brain are, and how dramatically they differ from the perception we might have as owners of brains. The harnessing of experience-based plasticity for the benefit of rehabilitation will most likely require research for many years yet to come and I truly hope to be able to continue to be a humble part of it.

Here and there, the reader may find references to the world of computers, which may seem odd at first glance. However, given my 20 years of experience in software engineering and computing, I tend to use computer and software architecture as a way of comprehending how intricately and indeed differently, nature has implemented programmable and adaptive mechanisms. I beg the reader's forgiveness for slipping into the language of my past, now and again.

Inge Wilms, August 2011

For my Dad, who instilled in me a love of science. I wish you were here.

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Also many thanks to the people who volunteered as test subjects, my colleagues and patients at Center for Rehabilitation of Brain Injury, colleagues at the Center for Visual Cognition, students, family and friends.

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Last but not least, my venture into the world of science and research would never have been possible without the loving support and constant encouragement from the two people who means the most to me, Carsten and Kevin, who never stopped believing in the project. I love you both.

Inge Wilms,

Allerød, August 2011

## **Abstract in English**

The overall theme for the studies performed as part of this Ph.D. project was to study aspects of the use of advanced technology in rehabilitation after brain injury. In particular, adaptation mechanisms related to feedback during training.

This Ph.D. thesis consists of three papers, one in press, and two published. In addition to the papers, the thesis includes a thematic presentation of fields in which the studies are positioned. Furthermore, the theoretical part includes results from a study yet to be published.

The thesis investigates two aspects of feedback in relation to experience-based plasticity. The first aspect is how the format of feedback influences the visuomotor adaptation to a visual distortion induced by prism goggles. The two studies included in the thesis indicate that the format of feedback influences the size of the adaptive effect measured by the so-called after-effect. The largest after-effect is achieved when subjects are allowed to see the tip of their finger as direct feedback on pointing precision during prism exposure. Indirect feedback, such as an “X” on a computer-screen and even images of fingertips, results in smaller after-effects.

The second aspect being investigated is how a training program for rehabilitation may adapt level of difficulty and training progression through a feedback loop during training. The study demonstrates that artificial intelligence algorithms are able to control a set of parameters each of which represents a potential aspect of difficulty. Reinforcement algorithms are used in the direct and online processing of feedback per trial and the results are used to select the properties of the subsequent action. This advanced computerized control of different elements of difficulty facilitates a more flexible modulation of progression and presentation of level of difficulty in relation to the abilities and learning progress of a patient.

The feedback studies emphasize that rehabilitation may benefit from the use of technology but also caution researchers that seemingly insignificant changes in implementation or execution of computer-based training may elicit quite different results. The third paper in the thesis focuses on this particular aspect of technology in rehabilitation.

## Dansk Resumé (Abstract in Danish)

Det gennemgående tema for Ph.D. projektets studier er brugen af avanceret teknologi i rehabilitering efter hjerneskade med særligt fokus på tilpasningsmekanismer i forbindelse med genoptræning.

Denne afhandling er en artikelbaseret afhandling bestående af tre artikler, den ene under udgivelse og de to andre publiceret. Afhandlingen består af en sammenfatning, som indleder artikel sektionen og positionerer studierne i forskningsmæssig sammenhæng.

Sammenfatningen inkluderer desuden et endnu ikke udgivet studie, som ligger i forlængelse af de udgivne resultater.

Afhandlingen undersøger to aspekter af feedback i relation til erfaringsbaseret plasticitet. Det ene aspekt er, hvordan formatet af feedback øver indflydelse på visuomotor tilpasning til forskydninger i visuel input forårsaget af prisme briller. De to studier i denne del af afhandlingen indikerer, at formatet af feedback influerer på størrelsen af tilpasningen, udtrykt ved den såkaldte "after-effect". Den største effekt opnås, når forsøgspersoner modtager feedback på pegepræcision (under påvirkning af prismeforskydning), ved at se deres egen fingerspids. Indirekte former for feedback, så som "X" på en computer skærm og billeder af fingerspidser, giver anledning til en mindre effekt.

Det andet aspekt er, hvordan et træningssystem automatisk kan tilpasse niveauet for træning direkte baseret på kontinuert feedback fra patienten under træning. Studiet viser, hvordan kunstig intelligens kan benyttes til at styre tre parametre, der tilsammen bestemmer træningens sværhedsgrad og konstant tilpasses patientens nuværende evner og præstationsniveau.

Feedbackstudierne understreger, at rehabilitering med fordel kan drage nytte af avanceret computerteknologi, men også at dette skal gøres med omtanke. En tilsyneladende ubetydelig ændring i opbygning eller udførelse af computerbaseret træning kan medføre ganske betydelige forskelle i effekten af træningen.

Den tredje artikel i afhandlingen fokuserer på dette særlige forhold i anvendelse af avanceret teknologi i sammenhæng med erfaringsbaseret plasticitet.



## Introduction

A fundamental element of adaptability is the ability to respond to feedback. Feedback allows us to detect a discrepancy between the planned activity and the actual outcome, no matter the cause of the discrepancy. Feedback may be immediate, when we fail to grasp a target, or delayed, when we fail to grasp the assembly instruction for furniture from Ikea. Feedback may be provided for conscious reflection and subsequent conscious modification of behaviour as when a student gets a report back from a teacher, or it may be subconscious as when the visuomotor system tracks movements towards a target. In experience-based plasticity, the feedback mechanism may be considered one of the fundamental elements in the process of change and learning.

The studies in this thesis focus on ways feedback may be used to harness experience-based plasticity in relation to rehabilitation training after brain injury. The results from three experimental research studies have been selected for inclusion, two on feedback in relation to adaptation to distorted visual input (PAPER 1 and STUDY 4) and one on feedback in relation to training controlled by artificial intelligence (PAPER 2). The results from the first research study have been published in PAPER 1 “Indirect versus direct feedback in computer-based Prism Adaptation Therapy” (Wilms & Malá, 2010). The results from the second study (STUDY 4) have not yet been published, but have been included in the thesis in chapter 4, as they further expand on the findings in PAPER 1. The results from the third study have been published in PAPER 2 “Using Artificial Intelligence to Control and Adapt Level of Difficulty in Computer- Based, Cognitive Therapy – an Explorative Study” (Wilms, 2011).

An underlying theme of the thesis is the use of advanced technology in rehabilitation and how controlled interaction between human and computer may be a way forward in harnessing experience-based plasticity. The third paper, PAPER 3 (Wilms & Mogensen, 2012), theorizes on the subject of technology used in the attempt to re-establish functional integrity after brain injury. Even though the use of technology may provide new and hitherto unknown data about the relationship between brain injury and functional impairment and improve access and content of training, it also challenges our interpretation and translation of data. As PAPER 1 and STUDY 4 demonstrate, what seemed like a mere conversion of prism

adaptation therapy to a computer-based setting introduced changes which affected experience-based plasticity. Essentially, computers do only what they are programmed to do placing a huge responsibility on the designers and programmers converting research knowledge into computerized assessment and training systems within the boundaries of technology. In turn, careful observation of the results from computer-based interaction may reveal further information on the mechanisms of recovery.

### **The structure of the thesis**

This thesis is comprised of two main parts: 1) a thematic section which positions the studies of this thesis within cognitive rehabilitation research, identifies the discoveries, discusses the results, and reflects upon the implications for future research; 2) a series of research papers published or accepted for publication.

### **The Thematic section**

The thematic section serves to position the studies and the results of the thesis within the scientific framework of cognitive rehabilitation research. The studies focus on the role of feedback from two different angles, both of which relates to adaptation in relation to experience. Chapters 1-4 deal with the study of feedback in relation to the adaptive mechanisms of experience-based plasticity of the brain positioning PAPER 1(Wilms & Malá, 2010) and unpublished data from STUDY 2. Chapters 5-6 deal with feedback in relation to adaptive mechanism in a computer-based training program positioning PAPER 2 (Wilms, 2011).

A final chapter, chapter 7, sums up the results emphasizing that cognitive rehabilitation research is a constant oscillation between clinical applied research aimed at improving techniques and basic research aimed at understanding the fundamental aspects of the deficit and ultimately the brain itself.

Throughout the text, the brain is sometimes being referred to as a subject in itself. This is not to imply that the brain has a life of its own separate from the rest of the body or the individual. It is merely done to simplify reference to processes happening in this particular organ.

### The Paper section

This section consists of three original publications:

1. PAPER 1: “Indirect versus direct feedback in computer-based Prism Adaptation Therapy”, published 2010 in Neuropsychological Rehabilitation (Wilms & Malá, 2010).
2. PAPER 2: “Using Artificial Intelligence to Control and Adapt Level of Difficulty in Computer-Based, Cognitive Therapy – an Explorative Study”, published 2011 in Journal of Cybertherapy and Rehabilitation (Wilms, 2011).
3. PAPER 3: “Dissimilar Outcomes of Apparently Similar Procedures as a Challenge to Clinical Neurorehabilitation and Basic Research - when the Same is not the Same”, accepted for publication in Neurorehabilitation, accepted for publication (Wilms & Mogensen, 2012).

## Chapter 1 – Experience-based brain plasticity

*“When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased” (p. 62) (Hebb, 1949).*

Observing children overcoming acquired brain injury, Donald Hebb wondered about the mechanisms of the brain that would enable such recovery and leave the children with little or no apparent mental difficulties (From Cooper, 2005). Inspired by the work of contemporary peers like Lorente de Nò and Karl Lashley as well as his own work within development and learning, Hebb hypothesized that the pressure of experience somehow affected the neural substrate of the brain in the manner captured by the famous postulate above (Cooper, 2005; Hebb, 1949). Over time, this very simplified view of the intricate mechanisms involved in experience-based plasticity has been expanded to include not only the synaptic increase in effectiveness but also the synaptic weakening in response to decreased activity. Today, Hebbian plasticity mechanisms of long-term potentiation and long-term depreciation form the basic understanding of most cognitive models of learning and memory (Abbott & Nelson, 2000). Furthermore, it has been firmly established that experience-based plasticity is the foundation for learning and adaptation throughout life (e.g. Hensch, 2005; Kleim & Jones, 2008; Mogensen, 2011a, 2011b; Ward, 2005). Experience-based plasticity may be accomplished through a range of different mechanisms and this first chapter provides an overview of the mechanisms and how they may be employed in the recovery of cognitive function after brain injury. Brain injury in this context refers to sudden non-progressive injury sustained to a previously healthy brain, primarily through trauma, ischemia, thrombosis or haemorrhage.

### Fundamental learning and adaptation

Experience-based plasticity has been defined as the ability of the nervous system to respond to intrinsic or extrinsic stimuli through a reorganization of its internal structure (Cramer et al., 2011) primarily believed to be the result of long-term synaptic and axonal changes in the neural substrate (Abbott & Nelson, 2000). This reorganization may be observed in various way, e.g. as regional changes in weight and volume of the neural substrate subserving a function (e.g. Rosenzweig & Bennett, 1996) as well as localized changes in metabolism on

fMRI imagery (e.g. Thimm, Fink, Kust, Karbe, & Sturm, 2006). In 1985, Rumelhart & McClelland (1985) proposed that the data carrying structures in the brain were organized in neural networks in which memory was stored across a landscape of interconnected neurons, each contributing to the storage and retrieval through weighted modulation. Learning was defined as a basic weight adjustment in the network based on the statistical propensity between input and output stimuli through feed forward and feedback realignment. By adjusting individual weights for triggering activity in the neuron, a group of neurons would be able to express complex behaviour beyond the ability of the individual parts of the network.

Computer implementations of the theoretic neural network models have substantiated that these mechanisms may in fact produce implicit structures or “knowledge” capable of reacting with sensible output given a certain set of input stimuli (McClelland & Rumelhart, 1987). Computer models, however, bear only superficial resemblance to the implementation of the neural networks of the brain as computer models cannot be considered plastic by nature. Whereas computers have a distinct separation between software and hardware, the brain has no such sharp delineation. The neural substrate of the brain, serving as hardware, software and data storage, is able to learn and adapt to internal and external stimuli through the mechanisms of experience-based plasticity (Mogensen & Malá, 2009).

Figure 1 illustrates how the brain may organize and strengthen connectivity and activation of individual elements of the network through feedback mechanisms. Figure 1 is my simplified model of how repeated training of a skill may induce changes that improves the effectiveness and fluency of said skill. The model depicts an untrained network (1), and how it changes in response to focused, repeated activity (2). Increased and constant activity will produce stronger and faster connections between nodes in the network (3) and reduce the dependency on lesser pathways (4) which will then be reduced (5). It suggests that what would normally be considered the hardware layer - and as such fixed - is in itself an adaptable entity influenced by continued training and stimuli.

# Neural Network Learning

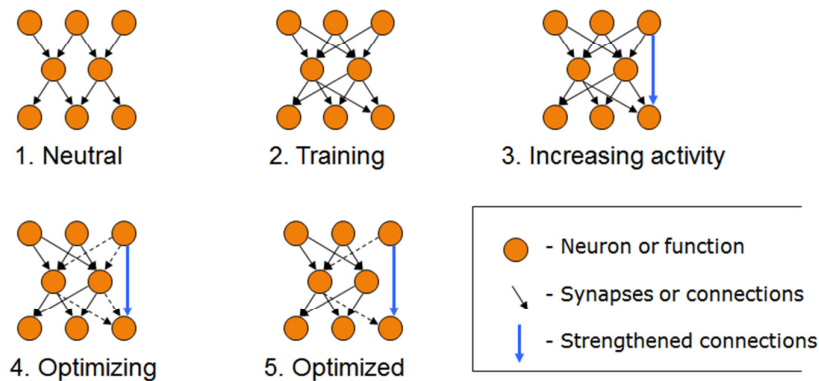


Figure 1. The taxonomy of skill learning at the neural level. The circles indicate neurons or clusters of neurons connected through synapses or axons. As training increases, the connectivity between active areas is increased and optimized by constant stimulation (adapted from (Robertson & Murre, 1999)).

The model above is an overly simplified representation of the current knowledge and principles of experience-based plasticity, but it hopefully serves to illustrate that the acquisition of a skill, be it motor based or cognitive, is more than just new or optimized programming on top of existing available hardware.

The model is a way to summarize the following points relevant to the later chapters and the studies in this thesis. Firstly, that the internal organization needed for interaction in the neural substrate is formed or honed in response to activity and experience; secondly, that the organization of the neural substrate may be accommodated internally in a manner which may differ from individual to individual although the surface behaviour may seem similar. Considering that the learning and honing of skills take an individual course for each of us, no two people are likely to achieve a skill in precisely the same manner. Thirdly, that skill is imbedded in an intricate structure which is neither hardware nor software as we know it from the computer world. The three points help to illustrate the challenge and the complexity facing anyone trying to isolate the effect of an injury and subsequently attempt to define a path for recovery of an impaired skill.

## Brain injury

In Denmark, approx. 22.000 people a year are surviving injury to the brain. The most common causes of injury are ischemic attacks, haemorrhage and head trauma but also illness and anoxia may cause lasting non-progressive injury to the brain (Sundhedsstyrelsen, 2011). At the neurophysiological level, initial destruction from obstruction of blood flow or disease may cause damage and loss of neural substrate serving as basis for cognitive as well as motor functions. This includes destruction of neurons and synaptic connections as well as axonal pathways between more distant areas of the brain. This in turn may cause further disruption due to imbalance in signals caused by lack of inhibitory or excitatory signals from the destroyed areas (Cramer, et al., 2011). Lack of inhibitory signals from extinct or damaged areas may cause overexcitement of other areas causing erratic firing or response to stimuli. Destruction or reduction in neural pathways may cause asynchronous data processing resulting in slow or delayed processing of incoming stimuli. Circuitry unaffected by the physical injury itself may be affected by the erratic feedback signals, as have been observed in cases of neglect (Redding & Wallace, 2006).

The brain keeps internal maps of the topography of the body and the surrounding world in order to determine the spatial coordinates of objects and stimuli (Redding, Rossetti, & Wallace, 2005). These internal representation may also be affected by injury causing invalid translation and response to feedback stimuli and consequently invalid learning and adaptation (Ramachandran & Hirstein, 1998; Ramachandran & Rogers-Ramachandran, 1996). After the injury, the adaptive learning mechanisms of the brain will continue responding to stimuli even though they may be considered erratic responses to initiated action. This faulty adaptation may lead to a state called learned non-use, where parts of the brain and the subsequent motor control become dormant due to initial decrease in motor feedback during the initial phases of brain injury (Pulvermüller & Berthier, 2008; Taub, 2004; Taub & Uswatte, 2006).

Figure 2 depicts two types of injury to the neural network from Figure 1. In the first case (6.a), the network pathways between two areas are severed leaving only small and decrepit pathways which delays or completely prevents the signals between two components of the network. In the second case (6. b), the pathways are more or less intact but the foundation

of the function has been diminished or destroyed. The point I want to make is that the intricate neural network established through experience and training, is ripped apart and the foundation for execution of a skill is impaired with bits and pieces still responding to signals and stimuli. This foundation for relearning and rehabilitation is dramatically different from the foundation present when learning a new skill in an uninjured brain.

## Neural Network and Brain Injury

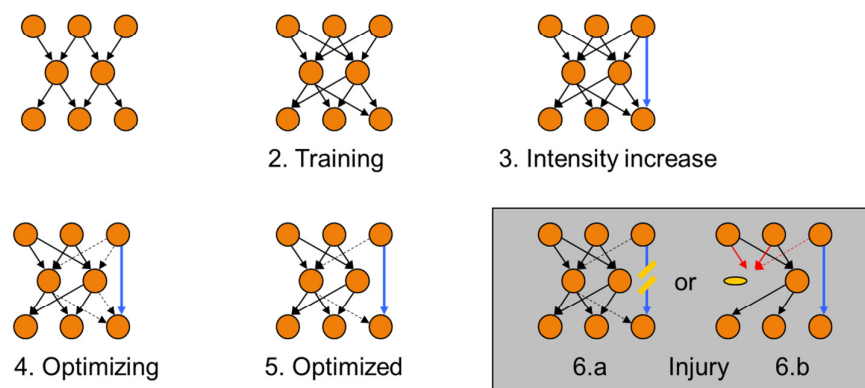


Figure 2. Graphical example of types of injury to the foundation of the neural network from figure 1 (adapted from (Robertson & Murre, 1999)).

### The role of experience-based plastic in recovery from brain injury

The hypothesis that the plastic mechanisms of the brain induce change as a result of experience and activity has fuelled extensive research into understanding the nature of these mechanisms and the conditions for their control and harnessing (Cramer, et al., 2011; Duffau, 2006; Kleim & Jones, 2008; Robertson & Murre, 1999). In rehabilitation research, knowledge about experience-based plasticity has slowly but fundamentally changed the perception that injury to the neural substrate of functions of the brain would result in final and permanent impairment. Previously, it was believed that full or partial recovery from injury mostly happened spontaneously in response to the de-swelling of brain tissue improving blood flow to affected areas. Now, increasing amount of evidence supports that experience-based plasticity may be a major factor in the recovery from acquired brain injury. In a study of the impact of training, Kim et al. (2009) compared a group of healthy subjects to a group of TBI patients with attention problems. The TBI patients were subjected to 4



weeks of attention training, and improvements in speed and accuracy were measured using a modified Posner test after completed training. In the subsequent fMRI comparisons, the TBI patients had significantly more activation in frontal and temporoparietal lobes and less in the anterior cingulate gyrus, temporoccipital region and supplementary motor areas compared to healthy controls. These changes were not present before training indicating that attention network resources were susceptible to experience-based plasticity and the mechanism of recovery included activation of alternative resources.

Another mechanism of experience-based plasticity is the reactivation of neural substrate rendered dormant due to “learned non-use” (Meinzer & Breitenstein, 2008; Meinzer et al., 2008; Pulvermuller et al., 2001; Pulvermüller & Berthier, 2008; Taub, 2004). Taub et al. (1999) had observed that a temporary disruption or depression of motor activity due to injury would reduce the use and function of upper extremities after recovery. He demonstrated that subsequent brief and intensive training forcing the use of the affected limb would indeed improve voluntary control and function. Similar effects have been demonstrated in rehabilitation of aphasia (Pulvermuller, et al., 2001) and further studies have indicated that maladaptive plasticity may be responsible for learned non-use and that the effects can be reversed through training (Breier, Maher, Schmadeke, Hasan, & Papanicolaou, 2007; Maher et al., 2006; Nudo, Plautz, & Frost, 2001; Sterr & Saunders, 2006). Experience-based plasticity has also been demonstrated in the reorganization of the internal topological maps which models our body in relation to the world around us and allows a correct interpretation of the origin of sensation or calculation of the position of objects (Ramachandran & Hirstein, 1998; Fernandez-Ruiz, 2006; Ward, 2005; Wallace and Redding, 2005; Gauthier, 2008).

Experience-based plasticity, as a mean for recovery after brain injury, offers hope for future rehabilitation therapy, but the task of determining the training required to alleviate the effects of injury, based on the relationship between the injury location and the expression of the functional impairment caused by the injury, is daunting. In addition, recovery from brain injury may be defined differently depending on perspective. If skills are considered to be tools needed to solve a task then, on the surface level, recovery from injury is the reinstatement of the ability to execute the now impaired task. Viewed in this context, vocal

speech is a tool for communication. Since, communication can be achieved through other means that vocal speech e.g. using writing or artificial speech generation, recovery in this sense might be achieved by training other ways to communicate. If, on the other hand, the production of speech is considered to be a task, vocal speech recovery would be understood as the reestablishment of the ability to speak. The training in this case would be aimed at recovering the sub-skills needed in the production of speech.

Another challenge is the apparent paradox that the destruction of the neural foundation for a skill or function does not permanently damage the ability to express the skill at the surface level. The REF (Reorganization of Elementary Functions) model attempts to bridge the apparent paradox that destruction of the neural substrate in an area known to subserve a specific function may not result in total inability to express the function (Mogensen, 2011a, 2011b; Mogensen & Malá, 2009). In this model, the observed expression of a function may be accomplished through activation of different combinations (Algorithmic Strategies or AS) of elementary subfunctions. Training is required to establish new AS combinations of elementary subfunctions and in this way, training shapes and develops and to an extent also limits the skilled ability. At surface level, improvements to a specific skill may be observed, but internally, the observed results are now mediated through the activation of novel combinations of subfunctions.

So planning a path for recovery requires not just knowledge of how a healthy brain executes a task, but also knowledge of the internal or external resources available to training and how best to shape the training to support the mechanisms of experience-based plasticity.

### **Plasticity and feedback**

Experience-based plasticity is not just explicit learning in the sense that learning is under cognitive and conscious control. Experience-based plasticity may occur automatically and implicitly as demonstrated by Pavlov's (1927) most famous study with classic conditioning of dogs. The actual feeding of the dogs happened to coincide with the sound of a bell and over time the sound of the bell alone would elicit drooling response similar to that of actual feeding. The timing of stimuli from two otherwise unrelated activities may be inadvertently learned to signify the same activity.

In educational research feedback has been defined as information on aspects of one's performance or actions, provided by an agent (e.g. a parent, a teacher or a friend), which may assist in the adjustment of action or activity to improve behaviour or skill (Hattie & Timperley, 2007). Feedback is recognized as playing an important role in the retention and long-term consolidation of knowledge (For review see Kulik & Kulik, 1988; Smith & Kimball, 2010). The temporal aspects of feedback in relation to explicit learning has been investigated in many studies related to formal education, (e.g. Kulhavy & Anderson, 1972; Kulik & Kulik, 1988; Mory, 2004; Rankin & Trepper, 1978).

In experience-based plasticity, feedback may be understood as the result from comparing the expected outcome of an action with the actual outcome (Magescas, Urquizar, & Prablanc, 2009). Discrepancy which hampers the execution of a task will result in an attempt to adjust parameters of the action. In the area of e.g. visuomotor control, sensory feedback from visual and tactile channels may be used in a constant action-feedback loop to correct trajectory of limbs during movement. A failure of precision may also be detected at the end of a movement in which case the internal representations or parameters for similar future movements will be adjusted before re-initiation of action (Adams, 1987; Cameron, Franks, Inglis, & Chua, 2010).

PAPER 1 and STUDY 4, in this thesis, demonstrate that the actual presentation of feedback may also influence the way the visuomotor system adapts to changes in visual input. The studies indicate that the property of feedback and not just the timing influence the experience-based plasticity of visuomotor adaptation to visual input distorted by prism goggles. Chapter 4 will expand further on the details of the findings.

## Chapter 2 - Neglect

### Introduction

It was in the middle of winter when Mrs P. appeared at the research department at Center for Rehabilitation of Brain Injury for the first time. She was a textbook neglect patient with the right side of her face and hair neatly made-up and with the left side in complete disarray. She wore warm winter clothes, but on her left side she was bare-armed and totally unaware that her skin was exposed to the freezing cold. When asked to describe her problems, she only mentioned a problem she had navigating her wheelchair. After a period of extensive training, I met her again this time carrying a painting of the scenery from her garden. "I thought I'd made a great painting," she said, "and only when I moved back about 1,5 meters from the painting did I realize that all the ladybirds and flowers were placed in the right hand side. I now make a habit of moving back and forth while painting, to make sure that the objects are evenly distributed on the canvas."

Neglect is a cognitive attention deficit that is defined as a failure to respond to, attend to, report, or orient toward stimuli presented in the contralesional side of space, which cannot be attributed to primary motor or sensory dysfunction (Heilman & Valenstein, 1972; Heilman, Valenstein, & Watson, 2000). Space, in this context, should be understood in the broadest sense of the word. It includes occurrences in the physical environment outside an arm's reach of the patients (extrapersonal space), the immediate surroundings (peripersonal space) and even the body (personal space) (Halligan, Fink, Marshall, & Vallar, 2003) and internal representations of body (the proprioceptive model) (Redding & Wallace, 2006). In a now famous study from 1978, Bisiach and Luzzatti demonstrated that even thought and imagination could be affected. When patients with neglect syndrome were asked to imagine that they were facing one end of a familiar central town square and describe what they saw, some would mention only landmarks to the imagined right side of the square. When the same patients were asked to imagine that they were facing the other end of the square, they would again describe only landmarks to the imagined right side. Neglect is a challenging syndrome in that it leaves the patient unaware of the consequences and effects of the impairment (Bisiach, Vallar, Perani, Papagno, & Berti, 1986). Patients, however, will often complain about the effects of neglect such as bumping into things, not being able to locate

objects in their homes or bruising the contralesional side of the body because of the inattention.

### Symptoms of neglect

Neglect is not a single impairment, but a multifaceted syndrome recognized by a collective of behaviours characterized by a difficulty to attend to lateralized stimuli. The most common behaviour of neglect patients is extinction, which is the inability to detect stimuli presented to the contralesional side, if stimuli are presented simultaneously to the ipsilesional side (Kinsbourne, 1987). Extinction has been demonstrated in different modalities with visual, auditive or somatosensory stimuli, either individually or in combination (e.g. Heilman & Valenstein, 1972; Karnath, Zimmer, & Lewald, 2002; Vallar, Bottini, Rusconi, & Sterzi, 1993).

In addition to a particular spatial domain, neglect may be observed from different midline-frames of reference (Figure 3), one being viewer-centered in which the neglected area is positioned relative to a midline projection from the retina, the head or the torso; the other being an allocentric reference frame where the neglected area is positioned relative to the stimulus or object (Medina et al., 2009).

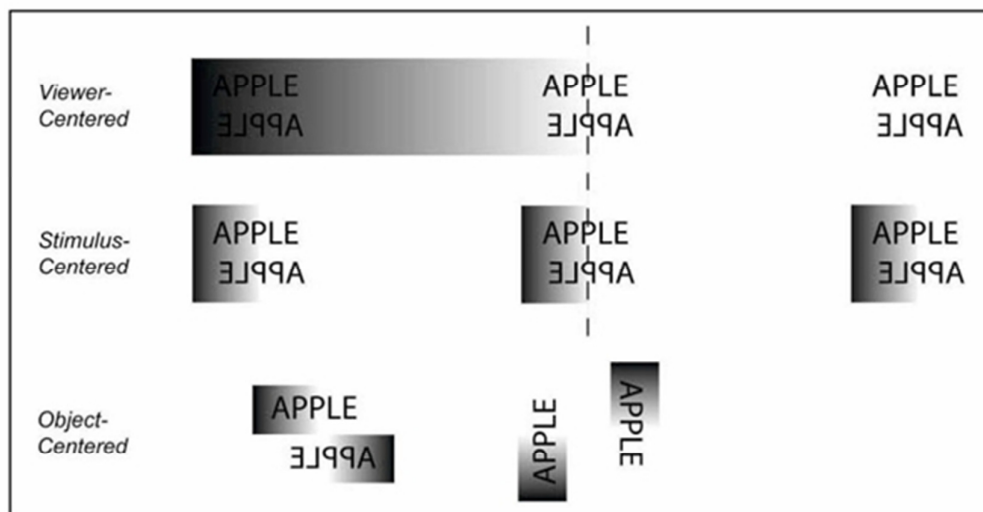


Figure 3. Patterns of performance of different types of unilateral spatial neglect. Dotted line refers to midline of the subject's body (from (Medina, et al., 2009)).

## Neural correlation of neglect

The diversity in neglect symptoms reflects the degree to which attention depends on different neural mechanisms (Szczepanski, Konen, & Kastner, 2010) and as a consequence different types of lesions may trigger one or more neglect behaviours. Neglect is often characterized as being a contralesional impairment and neglect is more frequently observed with right hemisphere damage than left hemisphere damage (Pedersen, Jorgensen, Nakayama, Raaschou, & Olsen, 1997; Ringman, Saver, Woolson, Clarke, & Adams, 2004; Stone, Halligan, & Greenwood, 1993). This asymmetry has so far been observed in humans only, giving rise to at least two attention models of neglect. The first is the representational model or hemispatial theory which proposes that the right hemisphere handles attention stimuli coming from both left and right attention space, whereas the left hemisphere only handles stimuli from the right attention space, partly because the language processes are thought to have cannibalized the neural capacity of the left hemisphere (Umiltà, Rizzolatti, Anzola, Luppino, & Porro, 1985). In other words, injury to the right hemisphere impairs the only place for left hand side stimuli to be processed and as a consequence neglect behaviour develops. The second model, the attentional bias model or interhemispheric competition theory, proposes that the left hemisphere is more biased towards right attention space than the right hemisphere is towards the left. Inhibitory networks balance the system under healthy conditions, but, when injured, the inhibitory signals from the contralateral hemisphere are lost or dampened causing overexcitement in the ipsilateral hemisphere leading to attentional bias (Cazzoli, Wurtz, Muri, Hess, & Nyffeler, 2009; Kinsborne, 1993; Mattingley, Bradshaw, Bradshaw, & Nettleton, 1994).

The most common cause of neglect are lesions to the right posterior parietal cortex (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005; Mishkin, Ungerleider, & Macko, 1983; Newport & Jackson, 2006) but also damage to the inferior temporal region and the superior/middle temporal gyri have been found to correlate with neglect (Buxbaum et al., 2004). In a very recent study of 55 patients with a focal right neglect, Verdon et al. (2010) found that damage to the right inferior parietal lobe was correlated with perceptive and visuo-spatial components of neglect. They also found that damage to the right dorsolateral prefrontal cortex was correlated to impairments in exploratory/visuomotor components and, finally, that damage to deep temporal lobe regions was a component of

allocentric/object-oriented neglect. Shirani et al (2009) tested 137 patients within 24 hours post onset and found evidence that hypoperfusion of the cingulate gyrus was the only significant indicator of viewer-centered neglect whereas hypoperfusion of the superior temporal cortex was strongly correlated with allocentric neglect. The latter is supported also by an earlier study by Hillis et al (2005); however, they found that hypoperfusion of the right angular gyrus correlated with viewer-centered neglect. Others (Chechlacz et al., 2010; Medina, et al., 2009) got different results, emphasizing the complexity in establishing distinct correlations between focal lesion and the various expressions of neglect.

## Prevalence

Neglect is a fairly common, cognitive impairment in patients with brain injury. The estimated incidence in the acute stages of brain injury varies significantly depending on the methods and standards for measurements used for screening; the inclusion criteria used; the motor skills and cognitive ability of the patient, and the timing of the assessment from onset (Bowen, McKenna, & Tallis, 1999; Edwards et al., 2006). In the UK, researchers found a prevalence of neglect ranging from 8% (Sunderland, Wade, & Hewer, 1987), in patients tested 21 days post onset, to 72% (Stone, et al., 1993) in patients tested within 2-3 days post onset. In the Danish Stroke study (Pedersen, et al., 1997), neglect was registered in 23 % of the acute population tested within 7 days post onset. In the US, Ringman et al (2004) found neglect, 24 hours post onset, in about 30 % of patients with evidence of lesions in CT scans but three months later only about 2 % of the same patients showed severe neglect behaviour and about 15 % showed moderate neglect behaviour. Across studies, there seem to be ample agreement that neglect behaviour fades rapidly, and after 3-4 weeks only approx. 8-10 % of patients will test positive for neglect (Sunderland, et al., 1987).

Long-term chronicity of neglect does not seem to correlate with sex, handedness or lesion volume but both the severity and persistence of neglect do increase with age (Gottesman et al., 2008; Ringman, et al., 2004). Right hemisphere lesions have been measured to cause neglect symptoms that are more persistent and less responsive to spontaneous remission (Buxbaum, et al., 2004) and therapy (Appelros, Karlsson, Seiger, & Nydevik, 2003). The severity of the neglect behaviour in the acute stages of injury has been found to be a strong predictor for the subsequent severity of symptoms a year post onset (Karnath, Rennig,

Johannsen, & Rorden, 2011). Finally, the presence of visual field disturbances and defects has been shown to be more prevalent amongst patients with chronic neglect (Karnath, et al., 2011).

### Neglect diagnostics

It is a challenge to assess a multifaceted syndrome like neglect, as the cause as well as the expression of neglect may vary from patient to patient. There exist many different diagnostic tests for neglect, some more sensitive to different types of neglect than others, but in general, there are no formal screening for neglect and no clearly defined recommendations as to which tests are best used in the initial diagnosis of the various subtypes. In the early phases of injury, neglect may go undetected as symptoms may be overshadowed by other impairments (Edwards, et al., 2006). In later phases, the symptoms of neglect are often less salient, as most patients have learned some sort of compensatory technique such as positioning their body or head differently when solving tasks. This may prevent correct assessment and even delay or prevent subsequent treatment to the distress of the patients. In research, the diversity and lack of commonality in the assessment of neglect has been raised as an issue as it complicates the comparison of results across studies (e.g. Bowen, et al., 1999; Buxbaum, et al., 2004; Cazzoli, et al., 2009; Hillis, 2006; Verdon, et al., 2010).

Another issue is the sensitivity of the most used standard paper-and-pencil assessments such as line bisection and star cancellation. My own observation is that often patients will report neglect-like symptoms when engaged in everyday activities like shopping, dressing, cooking and negotiating traffic but clear the score of commonly used assessments with no problem. Studies of the performance during assessment, however, have revealed that even patients, who have clinically recovered from neglect, may use a different approach in solving tests like the baking tray test (Appelros, Karlsson, Is, Tham, & Nydevik, 2004; Tham & Tegner, 1996), the line bisection test (Tseng, Diedrichsen, Krakauer, Shadmehr, & Bastian, 2007) and star cancellation test (Broeren, Samuelsson, Stibrant-Sunnerhagen, Blomstrand, & Rydmark, 2007). Computerizing assessment and scoring has been suggested as a way to increase the sensitivity of neuropsychological tests in neglect (Donnelly et al., 1999) and the recording of eye and hand movements during testing has been suggested as a way to increase knowledge and observations of aberrant behaviour which aids in detecting residual neglect impairments



(Guest, Fairhurst, & Potter, 2002). Vangkilde & Habekost (2010) recorded eye movements of neglect patients scanning images from the children's book "Find Wally" and detected subtle deviations in attention behaviour, before and after training.

Virtual reality applications of neglect tests are but the latest innovation within diagnostics. Currently, most solutions are basically translations of existing paper-and-pencil assessments with the purpose of increasing precision and the recording of data (Baheux, Yoshizawa, Seki, & Handa, 2006; Fordell, Bodin, Bucht, & Malm, 2011; Kim et al., 2004). However, new tests are emerging which use the safety of the virtual reality environment to place patients in simulated real-life situations, like wheelchair (Buxbaum et al., 2008) or traffic navigation (Kim et al., 2010; Weiss, Naveh, & Katz, 2003), and measure their reaction.

However, it must be pointed out that introducing advanced technology does not just provide benefits, it also adds to the complexity as it changes the conditions for the execution of test and therapy. As indicated in PAPER 1, PAPER 3 and STUDY 4 of this thesis, even seemingly insignificant disparities between standard training and computer-based training may change significantly the way experience-based plasticity responds to the therapy. Careful testing and evaluation are therefore required to ensure that a paper-and-pencil version and a computer-based version of the same assessment both produce similar results and if not, results should be analysed to detect why not.

As the knowledge about neglect in relation to experience-based plasticity improves and the correlations between lesion types and subtypes of neglect are better understood, hopefully new tests will be established which are better suited for the planning of treatment and therapy.

### **Neglect rehabilitation**

Rehabilitation has been defined as a process whereby people disabled by injury or disease work together with professional staff, relatives, and members of the wider community to achieve their optimum physical, psychological, social, and vocational well-being (Wilson, 2008). This definition covers a range of rehabilitation initiatives including training.

The multitude of underlying causes of neglect and the difficulty in assessment are reflected in the approach to training and therapy. No single treatment has been demonstrated

effective for all types of neglect (Ting et al., 2011), and a recent Cochrane review from 2007 (Bowen & Lincoln) concludes that no rehabilitation approach for neglect are yet supported by evidence from randomized trials. In the latest report on rehabilitation from brain injury from the Danish Board of Health (Sundhedsstyrelsen, 2011), an analysis based on 17 papers concludes that best effect of treatment of neglect is achieved through a combination of therapies.

There seems to be general consensus to make a distinction between neglect therapy relying on top-down processes (goal driven under conscious control) and therapy relying on bottom-up processes (stimulus-driven, mostly relying on implicit learning mechanisms) (e.g. Adair & Barrett, 2008; Marshall, 2009; Robertson & Murre, 1999). Examples of successful top-down based therapies include visual scanning therapy, in which the patient is trained in voluntary direction of the eyes towards the left with or without the use of aids (e.g. Katz et al., 2005) and limb activation where patients are encouraged to make movements with the impaired part of the body (Robertson, McMillan, MacLeod, Edgeworth, & Brock, 2002). Successful bottom-up strategies include neck vibration therapy (Karnath, Christ, & Hartje, 1993; Schindler, Kerkhoff, Karnath, Keller, & Goldenberg, 2002), optokinetic stimulation, in which patients are asked to attend to stationary targets on a background moving towards left (Kerkhoff, Keller, Ritter, & Marquardt, 2006; Pizzamiglio et al., 2004; Schroder, Wist, & Homberg, 2008) and prism adaptation therapy which will be dealt with in detail in chapter 3.

One challenge in all therapy and training is the lack of efficient, precise, ecologically valid functional recovery measures. This is not unique to area of neglect but a concern across the field of cognitive rehabilitation (Donovan et al., 2011).

As illustrated by the case of Mrs P at the beginning of the chapter, she was initially unable to dress and comb her hair properly. Several approaches were chosen to rehabilitate Mrs P, one of which was to make her aware of the deficit and its consequences. By learning to perform conscious actions of attention, like regularly checking the canvas at different distances, she was able to assume her long-time passion of painting. Hair combing success, however, continued to depend on the kind feedback from her husband. In addition to physical therapy, Mrs P. was also exposed to prism adaptation therapy.

## Chapter 3 - Prism Adaptation Therapy

For more than a century, prism adaptation has been used to study experience-based plasticity and in particular, how the visuomotor system adapts to the visual distortion created by the prisms. Stratton (1896) was the first to test if the angle of the retinal projection of the visual image was a determinant for the subsequent perception, by rotating visual input 180 degrees. He and others after him found that the brain will adapt to the distortion over time enabling the exposed subject to navigate and perceive the world as before.

### Prism Adaptation

Studies of experiential adaptation to optical transformations, like distorted input from the visual field induced by prism goggles or other external apparatus, have been conducted ever since using many different paradigms (e.g. Biocca & Rolland, 1998; Ewert, 1930; Harris, 1965; Redding & Wallace, 2001; Redding & Wallace, 2006; Stratton, 1896). In most prism adaptation studies, a temporary discrepancy between the internal representation and the actual position and extension of the body is created by letting visual input pass through prism goggles. The prism goggles cause a distorted projection depending on the angle and diopetre of the goggles (Figure 4).

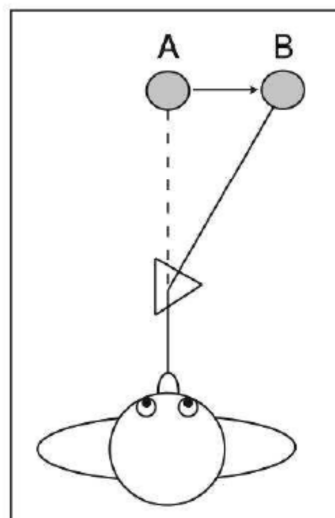


Figure 4. A prismatic right-shift causes targets in actual position A to appear to be at location B (Vangkilde, 2007). The diopetre of the prism goggles determine the angle of distortion. A prism diopetre of one will shift visual input 1 cm from A to B measured at the distance of 100 cm from the prism. This equals to 1.75 prism diopetre per degree. A ten degree shift requires a prism of 17.5 dioptries.

The typical research paradigm used for testing adaptation consists of three steps. The first step is an initial measure of the proprioceptive accuracy of the subject (without goggles), usually established either by letting the subjects point out the subjective midline repeatedly (Rossetti et al., 1998; Uhlarik & Canon, 1971) or by letting the subjects point to targets with the movement of their arm and hand disguised underneath a non-transparent barrier (blinded) (Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Redding & Wallace, 1988).

The second step is to expose the subjects to a visual distortion induced by the prism goggles. During exposure, subjects are provided with feedback on pointing precision allowing them to adjust to the exposure trial by trial. The degree of distortion may vary from study to study, but usually subjects will adjust to the visual distortion within a few trials, initially through conscious control (by forcing the hand to move further to the left than what seems natural) and after a while through more automated control (Redding, et al., 2005). As the motor control mechanism changes from conscious control to a level of more automated control, overcompensation can be observed for a brief period of time, causing a pointing deviation to the left of the target (Redding, et al., 2005; Wilms & Malá, 2010).

The third step is basically similar to the first step. Visual input is restored to normal by removing the prism goggles and the blinded pointing precision is re-measured. In healthy subjects, exposure to prism goggles produces an adaptation effect - the after-effect - that can be observed as a left-ward deviation in pointing accuracy once the prism goggles has been removed. The size of the after-effect correlates with the degree of distortion induced by prism goggles, the larger the deviation, the larger the size (Fernández-Ruiz & Díaz, 1999). Surprisingly, the average after-effect measured in degrees is almost always less than the distortion adapted to during exposure, residing at 40%-60% of the prism distortion. There is currently no explanation for this phenomenon. In my studies, I have observed total adaptation in a few subjects but have so far been unable to find any common factor like age, gender, physical condition or education amongst subjects that might explain this exception (Wilms, unpublished).

## Prism Adaptation as Therapy

In 1998, Rossetti et al. published a seminal study which demonstrated that exposure to prism adaptation might alleviate some of the symptoms related to egocentric visual neglect in patients, regardless of the severity of neglect. Internal data used to interpret sensory feedback from different modalities must be kept in alignment to ensure that action and attention are directed towards the same location (Bedford, 1993). Rossetti et al. hypothesized that the visuomotor realignment of the internal representation of the personal midline observed in standard prism exposure studies might alleviate symptoms of neglect. In their study, accuracy of blinded straight-ahead pointing was measured before and after 50 trials of target pointing during prism exposure to a 10 degree rightward visual shift. The results showed a marked improvement in straight-ahead pointing in the patients exposed to prism adaptation. Secondly, they tested the effect of the same prism exposure versus a sham procedure, immediately after adaptation and two hours later, using standard diagnostic neglect tests. Only the prism exposed group showed marked improvements.

Prism Adaptation Therapy (PAT) has since become one of the most promising therapies in the treatment of egocentric visual neglect (Frassinetti, et al., 2002; Serino, Barbiani, Rinaldesi, & Ladavas, 2009; Serino, Bonifazi, Pierfederici, & Ladavas, 2007; Vangkilde & Habekost, 2010). Usually, rehabilitation requires, to some extent, that the patient is aware of the impairment which least initially, patients with neglect are not. Even worse, the lateralized inability of the patient to orient towards incoming stimuli includes a more fundamental inability to detect the discrepancy between a planned action and the subsequent outcome and therefore affects some the normal adaptive mechanisms involved in recovery after injury. This would seem to pose a challenge in the use of experience-based plasticity in therapy. However, a key advantage of PAT is that it does not require the patient to be aware of his or her neglect condition, nor does it require cognitive control to maintain voluntary attention to be effective (Shiraishi, Muraki, Itou, & Hirayama, 2010). In standard PAT, the patient is exposed to prism distortion sessions, similar to the three steps described in the research paradigm above, twice a day for 2-3 weeks. Typically step one and three consist of 30-60 trials and step 2 consists of 90 trials of pointing. Most neglect patients are able to use the visual feedback implicitly to adjust their pointing activity (Redding & Wallace,

2006; Rossetti, et al., 1998), and poor adaptation during exposure is a strong indicator for poor neglect recovery (Serino, et al., 2007).

As in all rehabilitation research, however, clear and unambiguous results are difficult to achieve. PAT has been demonstrated many times to have immediate effect on the scores of standard neglect tests such as line bisection, star cancellation etc. (e.g. Dijkerman, Webeling, ter Wal, Groet, & van Zandvoort, 2004; Frassinetti, et al., 2002; Serino, et al., 2007; Shiraishi, et al., 2010). Some studies have confirmed long-lasting effect on visual neglect beyond 6 weeks in most patients when repeated for twice a day for two weeks (Frassinetti, et al., 2002; Serino, et al., 2007), others have found that the effect must be sustained by repeating PAT over time (Serino, et al., 2007) and others yet have found no long-term effect (Nys, de Haan, Kunneman, de Kort, & Dijkerman, 2008). It has been demonstrated that the effects may generalize into everyday life activities such as wheelchair navigation (Frassinetti, et al., 2002; Jacquin-Courtois, Rode, Pisella, Boisson, & Rossetti, 2008; Shiraishi, et al., 2010). However, in a semi random-controlled study by Turton et al. (2010), they found no improvements of daily self-care in 16 patients exposed to PAT compared to 18 patients exposed to sham treatment. As for the timing of the intervention, PAT has shown considerable effect as intervention in both the first period after injury and years post onset (Shiraishi, et al., 2010).

### **Prism adaption mechanisms**

In their model of visuomotor adaptation, Redding and Wallace distinguish between two types of corrections induced by the prism distortion - calibration and spatial realignment (Redding & Wallace, 2001; Redding & Wallace, 2002). Calibration is the fast, temporary and local rearrangement of spatial representations or parameters needed for planning and to some extent execution of a particular task. Spatial realignment is the slower alignment between several unique sensorimotor coordinate systems or spatial maps, which cause more long-term changes in the proprioceptive frames (for a complete review see Redding, 2005). In their model, the after-effect is the measure of the spatial realignment. When the arm is visible during the entire pointing movement (concurrent exposure or closed-loop exposure), little or no spatial realignment occurs during prism exposure (Redding & Wallace, 1988; Redding & Wallace, 2002). In contrast, terminal exposure (open-loop), where the

finger becomes visible at the very end of the movement or when reaching the target, creates the largest realignment after-effect (Redding & Wallace, 1992).

Experience-based plasticity does not require conscious control per se (Mogensen, 2011a) and adaptation to visual feedback has been demonstrated to be independent of visual awareness (Schenk, Schindler, McIntosh, & Milner, 2005), which benefits neglect patients who lack insight into their condition. The after-effect emerges even when the subject is not conscious of the visual distortion, if the distortion is introduced gradually (Michel, Pisella, Prablanc, Rode, & Rossetti, 2007). In our studies, subjects were always conscious of being exposed to the prism distortion, but this conscious knowledge did not in itself induce the visuomotor adaptation or reset it. Otherwise the removal of the goggles should have reset the after-effect immediately, which it did not.

In terms of experience-based plasticity, the after-effect may be used to measure the strength and degree of visuomotor adaptation (Fernández-Ruiz & Díaz, 1999). It has been demonstrated that the after-effect may in fact be the sum of several types of adaptation depending on the type of feedback provided during practice (Redding & Wallace, 1988; Simani, McGuire, & Sabes, 2007; Uhlarik & Canon, 1971). Recent studies have demonstrated adaptation to target errors (unpredictable changes in target location) differ from adaptation to internal misalignment (Diedrichsen, Hashambhoy, Rane, & Shadmehr, 2005; Newport & Jackson, 2006). Furthermore, it has been suggested that the perceptual part of the visuomotor system consists of several subsystems each of which rely on a spatial mapping, and that prism adaptation demonstrates the ability of the visuomotor system to maintain realignment between these subsystems involved in the pointing process (Redding & Wallace, 1992; Redding & Wallace, 1988). This supports that different adaptation mechanisms may be available depending on error type and feedback.

Pointing at a target is a visuomotor activity which is thought to involve the ventral stream in the identification of the target and the selection of the appropriate actions needed to fulfil the goal of pointing (Milner & Goodale, 2008). The dorsal stream is thought to use the current information about the egocentric coordinates to program and control the skilled movements needed to carry out the action (Milner & Goodale, 2008; Milner & Harvey, 1995). Studies by Smith et al. (2006) have demonstrated two distinct fast response patterns

to error detection, one being strong but short-lived and the other being weak but more durable suggesting that at least two distinct neural systems are involved in the adaptive processes. FMRI studies of the process have unveiled involvement of the anterior intraparietal sulcus in error detection and activation of the parieto occipital sulcus during error correction (Luaute et al., 2006; Luaute et al., 2009; Smith, et al., 2006) in healthy subjects.

### **Comments on feedback in prism adaptation**

Implicitly, sensory feedback plays an active role during execution of the movement towards the target in the online adjustment of the hand and finger as does the internal mapping or proprioceptive layout of the body and the position of its components in relation to real world objects. Fundamentally, adjustments to changes in the environment can only occur if the changes can be detected consciously or unconsciously as a continued discrepancy between the initiated action and the subsequent result (Bedford, 1993). However, since feedback is such an integrate part of the adaptation process it is rarely mentioned as a separate feature of prism adaptation. The properties of feedback presented as terminal exposure or end-point feedback has been investigated by Magescas et al. (2009) demonstrating that repeated online correction does not induce adaptation. Timing in relation to action feedback has been investigated (e.g. Beaubaton & Hay, 1986) and it has been demonstrated that delayed feedback produce weaker after-effects than immediate feedback (Shabbott & Sainburg, 2010). Feedback response has also been found to depend on whether the target is static or moving (Cameron, et al., 2010; Magescas, et al., 2009) and Redding and Wallace (2001) found that visual feedback from seeing the start position of a limb even influenced the locus of adaptation to distorted visual input.

So timing and presence of feedback have been studied to some extent but not the format itself. Many adaptation studies have been done in darkness with small LED light sources attached to the moving limb. The feedback has thus been restricted to being a light source, which experimenters could manipulate both in time and space (e.g. Bedford, 1993; Clower & Boussaoud, 2000; Henriques, Klier, Smith, Lowy, & Crawford, 1998; Rogers, Smith, & Schenk, 2009). However, by preventing subjects from getting direct feedback from seeing their actual finger, hand or arm, you may potentially engage different adaptation subsystems.



Likewise when presenting indirect feedback in the form of cursors on a screen or virtual limbs, you cannot be sure what visuomotor adaptation systems are activated. One recent study reported an initial experiment where screen cursor position used as feedback was changed to terminal exposure, because the learning curves using cursor feedback differed from those produced with terminal exposure (Tanaka, Homma, & Imamizu, 2011). The study offered no further explanation as to why this discrepancy occurred. In the next chapter, I will argue that it may make a difference whether feedback is presented as direct feedback or indirect feedback in processing and subsequent adaptation.

## Chapter 4 - The Feedback Studies

In an attempt to create a computer-based version of the equipment used for Prism Adaptation Therapy, a test was setup to verify that the computer-based version would produce after-effects similar to those produced by the standard PAT equipment. The results were not as we had expected and that initiated two studies to try to isolate the reason why.

A total of seven experiments have been conducted to investigate how changes in feedback affect the visuomotor adaptation to an induced distortion of visual input as measured by the after-effect. The first four experiments have been reported in detail elsewhere (PAPER 1), so here follows only a brief summary of these results. The results from the last three experiments (STUDY 4) have not yet been published and a more detailed account has therefore been included in this chapter. These experiments further investigate the property of feedback and how it influences the after-affect.

### PAPER 1 – experiment 1, 2, 3 and 4

In the first experiment, a group of 30 healthy subjects were exposed to one session of PAT under three different conditions. In the first condition, PAT was provided using the standard PAT equipment. During prism exposure, the subjects received feedback on pointing precision through terminal exposure i.e. seeing the tip of their own finger as they reached the target. In the second condition, PAT was provided using a computer-based implementation, where targets would appear one at a time at three different locations on a touchscreen. A wooden box in front of the screen would hide the arm movement as well as the fingertip. Subjects would receive feedback on pointing precision on the touchscreen in the shape of an “X”, which would be placed next to the target in a distance equal to the distance from target to actual pointing position underneath the box. In the third condition, the computer-based version of PAT was used, but this time subjects did not wear prism goggles during exposure but had to adjust to skewed feedback. Again, feedback was provided in the shape of an “X” but this time offset by 10 degrees to the actual pointing position. Under condition one and two, we observed similar learning curves during exposure. Each subject managed to adjust pointing movements to hit the actual target during prism exposure whether the feedback was the fingertip or the “X” on the screen. The after-effect, however, was notably different being considerably lower for the “X” feedback. Two other experiments were conducted to

test if it was indeed the difference in feedback and not some other experimental variation that was responsible for the measured difference in after-effect. They found no influence on feedback from other changes. A fourth experiment tested 7 patients with right hemisphere damage under two conditions with prism exposure, the standard wooden box and the computer-based solution with fingertip feedback. Each patient responded similarly to both conditions (Wilms & Malá, 2010).

## **STUDY 4**

As the results from the experiments in STUDY 4 have not yet been published, I will start with a presentation of the experiments and then propose a hypothesis based on the results from both PAPER 1 and STUDY 4.

### **Experiment 1– actual fingertip versus image of fingertip**

This experiment was conducted to test if it was the indirectness of the feedback rather than the category of feedback that changed the after-effect. 27 right-handed, healthy subjects (9 males, 18 females) with normal or corrected vision participated in this experiment. Subjects were recruited amongst the employees at the Center for Rehabilitation of Brain Injury (CRBI), and students of the Department of Psychology at the University of Copenhagen, Denmark. Subjects who had previously participated in prism experiments, subjects with severe visual dysfunction, or left-handed subjects were excluded from the study. All participants were tested using a computer-based session of PAT with feedback provided under two different conditions. Half of the group started with the first condition and half with the second condition based on a randomized sequence to avoid sequencing effect and both groups were tested under either of the two conditions a week apart. As in the PAPER 1 experiments, each participant was fitted with a plastic nail fixed with band-aid on the pointing finger to protect the touchscreen. The two conditions varied only with regards to how feedback on pointing precision was presented during the exposure trials. In the first condition, the subjects received direct visible feedback from the terminal exposure of their fingertip. In the second condition, an image of a fingertip was displayed right above the box, masking the arm movement, at the vertical position of the touching fingertip immediately after the subject hit the touch screen. The image was a photo of an actual fingertip with an artificial nail fixed to the finger with band-aid. To match the visual feedback from an actual fingertip, the fingertip on the image had been captured at three different angles roughly

matching the angle of the actual fingertip when pointing to one of the three target positions. The software selected the image with the best matching angle based on the actual touch position during the exposure trials.

Mean pointing precision was calculated from each step (pre, exposure and post) for each participant. The results were measured in pixels. A paired samples t-test showed no significant difference  $t(26)=-.691$ , two-tailed  $p=.496$  between the pre exposure measures of the direct feedback condition ( $M=-45.00$ ,  $SD=40.179$ ) and the image feedback condition ( $M=-37.93$ ,  $SD=51.305$ ). However, the after effect measured in the post exposure step showed a highly significant difference  $t(26)=-3.196$ , two tailed  $p<.001$  between the direct condition ( $M=-151.52$ ,  $SD=34.584$ ) and the image condition ( $M=-134.00$ ,  $SD=31.223$ ).

A repeated measures GLM showed no simple effect of method ( $F(1,26)=2.564$ ,  $p=.121$ ) nor was there any interaction effect between method and step ( $F(1,26)=2.045$ ,  $p=.140$ ). Since these values are higher than 0.0167, it can be concluded that there is a no significant difference in the mean scores from the after-effects of the two conditions overall. The mean and standard deviation of the after-effect were as follows: In the direct feedback condition ( $M=-151.52$ ,  $SD=34.58$ ) and in the indirect image feedback condition ( $M=-134.00$ ,  $SD=31.223$ ).

The data indicate that direct feedback from seeing the fingertip (terminal exposure) creates a slightly larger after-effect than seeing the image on the screen, but the observed difference is not as large as the one observed in Experiment 1 (see PAPER 1), where the indirect feedback was presented as an "X" on the touchscreen.

### **Experiment 2 –concurrent feedback versus terminal feedback**

This experiment was basically a simplified replication of an experiment reported by Redding and Wallace (1988), which compares the after-effect produced by the prism paradigm under two conditions. In the first condition, subjects view the complete arm movement during exposure trials and in the second condition, subjects receive only terminal feedback. The primary reason for replicating the experiment was to ensure that the research paradigm used in PAPER 1 and STUDY 4 would yield comparable results, even though this paradigm does not control for head movements. A secondary reason was to test if it shielding the arm

movement was crucial in also in computer-based PAT as the additional equipment needed for this would be inconvenient when offering PAT at the patients home location.

In the experiment, 31 right-handed, healthy subjects (7 males, 24 females) were tested under the two conditions a week apart. The equipment and general setup equalled those from STUDY 4 - experiment 1. The terminal feedback was provided by allowing subjects to see the tip of their finger when touching the target on the computer screen.

The results were measured in pixels. The same resolution was used as in STUDY 4 - Experiment 1. A paired samples *t*-test showed a significant difference  $t(30)=4.151$ , two-tailed  $p<.001$  between the post exposure measures of the concurrent exposure condition ( $M=-125.77$ ,  $SD=49.103$ ) and the terminal exposure condition ( $M=-153.48$ ,  $SD=40.700$ ). The results indicate that in this particular paradigm concurrent and terminal exposure do in fact produce after-effects of different size, thus replicating the observations of Redding & Wallace (1988). A very recent study confirms that the difference also are observed in actual treatment using PAT on a patient population (Làdavas, Bonifazi, Catena, & Serino, 2011), affirming that a change in treatment which might seem trivial surface level may have a rather large impact on the outcome of the intervention.

### **Experiment 3 –exposure to skewed feedback as either finger image or “X”**

In PAPER 1, the first experiment included a condition where subjects were exposed to skewed feedback rather than prism distortion during the exposure step. The original idea was to test if this would create an after-effect similar to the after-effect from prism exposure, thus removing the need for prism goggles during training. In the old study, the skewed feedback produced only half the after-effect, similar in size to the after-effect from the indirect feedback condition.

In this third experiment I wanted to revisit the skewed feedback condition. The result from the first experiment indicated that the after-effect produced by the direct feedback was almost similar to the after-effect produced by the indirect finger-image feedback (see PAPER 1). I therefore wanted to test if two types of indirect feedback would produce different after-effects. The expectation was that if the feedback provided by an image of a finger is

perceived similarly to feedback from a real finger, then I would also see a difference also in the skewed feedback paradigm which compares “X” to image feedback.

Thirty right-handed, healthy subjects (one male, 29 females) were tested under two conditions one week apart. The basic setup was similar to the previous two experiments as each condition consisted of a couple of test trials followed by 30 trials blinded measure of precision, 90 trials of exposure, and finally 60 trials measuring the after-effect. In both condition, the arm movement was completely hidden during all sessions. During the exposure step, subjects would not wear prism goggles but instead receive feedback on pointing precision which was shifted 10 degrees to the right of the actual hidden pointing position. In the first condition, the feedback would be the letter “X” and in the second condition, feedback would be the finger images used in STUDY 4, Experiment 1. The subjects would wear the artificial nail fastened with band-aid in both conditions.

The results were measured in pixels. The same resolution was used as in STUDY 4-Experiment 1 and 2. A paired samples *t*-test showed a significant difference  $t(29)=-2.308$ , two-tailed  $p=.028$  between the post exposure measures of the “X” feedback exposure condition ( $M=-97.67$ ,  $SD=33.035$ ) and the image feedback exposure condition ( $M=-112.57$ ,  $SD=33.035$ ).

Although adaptation to skewed feedback indeed differ from adaptation to a distortion similar in size induced by prism goggles, the fact remains that even using skewed feedback, a difference in reaction to the two types of indirect feedback can be demonstrated. This indicates that the difference in adaptation response is probably very fundamental.

## Discussion

In a study of the effect of feedback in virtual environments, displaying a hand image did not produce the same effect as seeing the real hand in a terminal exposure (Mason, 2007).

Movements were faster when feedback was provided by seeing ones actual hand. This may indicate that actual limb feedback is processed faster and perhaps more directly. My experiments demonstrate a difference in the way the properties of feedback influence experience-based plasticity as measured by the size of the after-effect. In PAPER 1, we speculated that the different reaction to feedback might be attributed to a difference in the

way the feedback was processed. Since the publication of PAPER 1, STUDY 4 has been conducted and the analysis of the results points towards a possible explanation and in the following, I will try to propose a plausible theory.

In 1992, Goodale and Milner (1992) suggested that visual input is processed in two different streams, the ventral (what) and the dorsal (how) visual pathway, each transforming visual information depending on the perceptual output requirement. Goodale and Milner were not the first to point to separate visual pathways for visual input, but they were first to propose a distinction between “vision for perception” and “vision for labour” related to the perceptual contribution of visual input in subsequent action (Milner & Goodale, 2008). According to their model, the perceptual contribution from the ventral stream is “the identification of possible and actual goal objects and the selection of appropriate action to deal with these objects” (ibid, p. 775). The perceptual contribution from the dorsal stream is in the implementation of the action as well as the “detailed specification and online control of the constituent movements that form the action, making use of metrical visual information that maps directly onto the action in the ‘here and now’” (ibid, p. 775). In other words, the dorsal stream plays no role in action selection but is critical for the execution and online correction of action. To do this, the dorsal stream relies on the subconscious data from bottom-up processes of visual input suggesting that at least online feedback is processed in the dorsal stream (ibid, p.780). Only highly practised and automated actions like pointing and grasping are likely to escape the intrusion from the ventral stream (ibid, p. 780).

I suggest that the direct feedback is processed by the fast dorsal stream which bypass conscious control and map actual perceived limb position to expected limb position. When the visual input has been diverted by prism goggles, the ventral stream issues a planned action and an expected result. The dorsal stream is used to execute and control the result from incoming feedback. The dorsal stream expects feedback to be a finger and not an indirect representation that basically requires conscious control and translation. So seeing a physical limb as feedback provides direct access to the visuomotor adaptation mechanisms whereas seeing an image, an X or other indirect representations on the screen depends on the ventral stream mechanisms for further interpretation and cognitive control. Since the

dorsal stream, according to Goodale and Milner, relies on the proprioceptive maps to correct movements online, the discordance between planned and actual result will be detected here.

More studies into possible delays in the reaction time to different types of feedback might be a way to further investigate this proposal.



## Chapter 5 - Advanced Technology and Cognitive Rehabilitation

As human brains can adapt to changes in stimuli, so can advanced computer software. The previous four chapters have focused on the role of feedback in relation to human learning and adaptation. The following two chapters deal with the use of advanced technology in rehabilitation training and therapy and focus on how feedback, in the interaction between human and computer, may be used to control software adaptation to the needs and deficits of the individual patient.

Starting with a brief history of the use of computer technology in rehabilitation, chapter 5 outlines the special challenges and pitfalls associated with use of advanced computer technology in cognitive rehabilitation positioning PAPER 2 and PAPER 3 in the thesis.

Chapter 6 deals specifically with the challenge of planning and controlling the progress in rehabilitation training to match the ability and progress of the patient. It sets the stage for PAPER 2, which demonstrates how artificial intelligence may be used to create a training environment, which is uniquely and interactively shaped to match the state of impairment and progress of an individual patient at any given time.

### A brief history

In 1968, *computer-assisted instruction* was being promoted at all major universities in the US with the specific goal of achieving individualized instructional education of students (Atkinson & Wilson, 1968). The idea was to let the student progress through a particular subject at an individual pace and route catering to the differences in ability and motivation. The expectation at the time was that the rapid technological development would take care of issues like the exorbitant cost of hardware, lack of random access storage devices, and limited access to computer mainframes. Time proved them right on these accounts, but Atkinson and Wilson raised another and more profound concern - the lack of theoretical background and common framework of metrics for the definition of learning goals and the subsequent evaluation of achievements. They correctly pointed out that an evaluation of a computer-assisted instructional system is partly an evaluation of the software and equipment being used but, more importantly, it is an evaluation of the software designer and how the stated learning goals have been translated and transformed into an instructional system based on computer technology (Atkinson & Wilson, 1968, p. 76). This

point has been raised again with standard computer-based training (Robertson, 1990; Robertson, 1999; Ting, et al., 2011) and in the use of virtual reality (Myers & Laenger, 1998; Rizzo, Buckwalter, & Neumann, 1997; Rose, Brooks, & Rizzo, 2005; Tsirlin, Dupierrix, Chokron, Coquillart, & Ohlmann, 2009). In other words, the development of a successful computer-based training system requires a system developer that understands how to combine training and learning strategies with the potential of advanced technology. Without a full understanding of the basic elements needed in training, the introduction of advanced technology is just adding further complexity into the equation.

Computer technology found its way into cognitive rehabilitation training in the early 80' with the advent of mini- and microcomputers. Even though the cost of equipment was exorbitant compared to today, it was recognized that technology could play a vital role in both the assessment of deficits, as a cognitive prosthetics, and as a way to offer cost effective treatment to more patients by improving the intensity, contents, and delivery of training (e.g. Dick, Wood, Bradshaw, & Bradshaw, 1987; Katz & Nagy, 1982; Loverso, Prescott, Selinger, Wheeler, & Smith, 1985; Mills, 1982). The reports from the 80's and early 90's demonstrate huge enthusiasm in the application of computer training within areas like aphasia (e.g. Katz & Nagy, 1982; Katz & Nagy, 1983; Mills, 1982), neglect (e.g. Bergego et al., 1997; Robertson, Gray, & McKenzie, 1988; Robertson, Gray, Pentland, & Waite, 1990), and memory deficits (e.g. Middleton, Lambert, & Seggar, 1991). The reasons for introducing computer technology in training then were basically the same as today - to increase therapeutic efficiency by providing easy and inexpensive access to therapy, to improve the content and quality, and to increase the intensity of therapy (Katz, 2009; Katz & Nagy, 1982; Rizzo, Schultheis, Kerns, & Mateer, 2004; Tsirlin, et al., 2009).

The benefits of computer usage was fairly quickly realized in the area of assessment, where the use of technology introduced improved and exact monitoring and recording of response time, accuracy and behaviour during assessment. Old and favoured paper-and pencil tests like line-bisection and cancellation tests in neglect have been converted to computer-based versions which have led to increased sensitive to the symptoms of neglect (Anton, Hershler, Lloyd, & Murray, 1988; Liang, Guest, Fairhurst, & Potter, 2010; Potter et al., 2000; Rabuffetti et al., 2002; Rengachary, d'Avossa, Sapir, Shulman, & Corbetta, 2009), as well as expansions

of said tests to include observations and assessment of aberrant behaviour (Baheux, et al., 2006; Baheux, Yoshizawa, Tanaka, Seki, & Handa, 2005; Broeren, et al., 2007; Donnelly, et al., 1999; Guest, Donnelly, Fairhurst, & Potter, 2004; Guest, et al., 2002; Rabuffetti, et al., 2002), and the detection and separation of multiple disorders (Beis, Andre, & Saguez, 1994). New assessment techniques have also been introduced e.g. with the use of virtual reality that, in addition to the recording and monitoring benefits, provide assessment opportunities situated in more realistic environments (Fordell, et al., 2011; Rizzo, et al., 2004). Last but not least, new meta test systems are being introduced, which are able to select the best assessment tools based on the actual performance of the patient during testing (Gur et al., 2010).

Assistive technology and compensatory rehabilitation are also areas which have embraced the use of technology (e.g. de Joode, van Heugten, Verhey, & van Boxtel, 2010). It is beyond the scope of this thesis to delve into all major accomplishments but memory aids (Wilson, Emslie, Quirk, Evans, & Watson, 2005), communicative devices (Fink, Bartlett, Lowery, Linebarger, & Schwartz, 2008; van de Sandt-Koenderman, Wiegers, Wielaert, Duivenvoorden, & Ribbers, 2007), and vision aids (Jutai, Strong, & Russell-Minda, 2009) are but a few of the examples.

Not surprisingly however, efficient use of computer technology in treatment has turned out to be much more difficult than other areas of use. It was established fairly quickly that computer-based mindless drill-training, in which the patients were made to repeat the same tasks over and over again, had little or no effect at all (Katz & Nagy, 1983). It was also observed that although the patients did improve on the task being trained, often no generalization or cross-over effect to activities of daily living was found (e.g. Katz, et al., 2005; McCall, Shelton, Weinrich, & Cox, 2000; Ramsberger, 2005). An early review in 1997 concluded that the effect of the training resulted from the language content of computer-based training and **not** from the mere use of the computer per se (Katz & Wetz, 1997). Another early review at the time, covering a wider range of cognitive treatments based on computer technology, concluded that efficacy of computer-based treatment did not differ from normal treatment (Chen, Thomas, Glueckauf, & Bracy, 1997). Others became so

desolate by the lack of results in computer-based treatment that they strongly cautioned the use of computer training pending further research (Robertson, 1990).

By the end of the 90's the initial excitement of using computers in cognitive rehabilitation treatment was replaced by resignation to the fact that computers in themselves did not solve the fundamental problems of cognitive treatment. As in 1968, researchers thirty years later began to realize that using computer technology to facilitate learning required standardized measurements of efficacy; treatment that was solidly based on learning and practice; better design and testing of user interfaces, and a deeper understanding of the mechanisms of the deficit being treated (Loverso, et al., 1985; Robertson, 1999).

### **Computer-based rehabilitation training today**

Today, there seems to be two main approaches to the use of technology in experience-based treatment. The first is to try to discover and understand every aspect of a deficit through detailed assessment and then develop specific solutions which train these aspects of the impairment. Prism Adaptation Therapy is one such example. The other is to accept that it may be well into the future before all aspects of brain injury are even uncovered let alone understood. Therefore, a different strategy is to develop therapy systems that model reality. With the introduction of virtual reality applications, it has become possible to emulate real world situations in a safe and controlled environment. It has so far been proven successful in teaching neglect patients how to navigate safely in traffic (Katz, et al., 2005; Kim et al., 2007), in training children with ADHD (Rizzo et al., 2006), and in desensitizing soldiers with PTSD (Rizzo, Reger, Gahm, Difede, & Rothbaum, 2009).

Brain-computer interaction is another field of technological development where signals related to a specific activity are monitored either intrusively with probes located near the activated brain areas (Coyle, Ward, & Markham, 2003; Friebs, Zerris, Ojakangas, Fellows, & Donoghue, 2004; Santana, Ramirez, & Ostrosky-Solis, 2004) or non-intrusively using advanced electroencephalography (EEG), fMRI or near-infrared spectroscopy (NIRS) (Curran & Stokes, 2003; Daly & Wolpaw, 2008; Sitaram, Caria, & Birbaumer, 2009; Vaughan et al., 2003). The feedback provided by the monitoring of brain signals is then used to check the progress of the experience-based plasticity resulting from changed behaviour.

Games technology is a third area that slowly has begun to interest researchers. Action computer games can keep people occupied with seemingly boring and trivial activities for hours on end, in the attempt to achieve rewards and skills. Most often, they contain elements of practice with increased levels of difficulty and they are set in environments that require activation of different cognitive skills, are motivating, and to some extent even addictive. More importantly, action games may model challenges, speed, progression and even general content to the particular preference of the gamer either stated explicitly through games parameters or implicitly by measuring the ability of the gamer (Charles & Black, 2004; Charles et al., 2005; Spronck, 2005). Many of these elements in games resemble to some extent those found to induce experience-based plasticity (Kleim & Jones, 2008) in computer-based therapy.

### **The Challenge of Individuality in Injury and Treatment**

Even though advanced technology has been available for some time and keeps inspiring to new and more exiting features of training and therapy, the fundamental issue of what type of training has an effect at which point in time is still unresolved. Training a new skill, cognitive or physical, require that the trainee progress through levels of training with increased difficulty and challenge (e.g. Kolb, 1983; Pulvermuller, et al., 2001; Rasmussen, 1983). In order to progress steadily, the trainee has to practise to achieve ease and precision in the execution of the skill (Kolb, 1983; Lave & Wenger, 1991). The same is basically true for many of our cognitive skills like speech, writing, problem solving etc. Although the complex neural foundation of cognitive skills is probably there from birth, many cognitive skills are honed during childhood and adolescence. The first challenge in learning a skill using computer technology is therefore to recognize the logical sequence of steps needed to acquire competency in general. Learning by doing or implicit learning is not achieved through cognitive reflection alone, if at all. The ability to execute a skill may require consistent and frequent use and practice not to deteriorate, but even a rusty skill can normally be recovered with a little practice.

However, a failing skill due to brain injury is not the same as the lack of a skill never learned. I believe that reclaiming a skill, impaired or destroyed by brain injury, may be more challenging for a number of reasons. They all have to be considered when attempting to

reconstruct the impaired ability, be it using computer-based or face-to-face therapy sessions. Firstly, there may still be traces of knowledge left or more precisely areas of neurons and connections that respond erratically to stimuli causing maladaptive learning. As mentioned earlier in chapter one, the lacking skill may be due to destruction of tissue both full and partial, destroyed or diminished network connectivity, asynchronous processing caused by slowed metabolisms, or even the lack of inhibitory or excitatory signals from other areas of the brain. The current state of diagnostics and assessment tools rarely, if ever, offer full details of what may be the underlying cause of the functional deficit. Secondly, no two injuries are the same and all patients are different. Motivation and goals for the individual patient may vary greatly dependent on the patient's ability, attitude, and even awareness of injury. As a consequence, what may be extremely difficult to one patient to master and achieve may be easy for another patient even though they have been diagnosed with the same impairment. Forcing patients to go through a fixed set of steps in training may in fact be counterproductive as the training may reinforce aberrant behaviour of the neural substrate. Thirdly, brain injury may cause fluctuation in performance due to fatigue and enhanced sensitivity to lack of sleep and changes in the environment. What may seem easy in one session may be very difficult in the next even for the same patient. It is here the challenge but also one of the benefits of technology in rehabilitation training presents itself. PAPER 2 and chapter 6 will expand on this particular aspect.

### **The same is not the same**

To create computer-based training systems, you have to define specifically what you think will have an effect based on rehabilitation models and theory and on observations from clinical practice. The detailed test and investigation required when building a training system will often reveal that what seems to be the same behaviour at a surface level may not always be so. Any implementation of computer technology is in essence a translation of ideas or practice into an automated environment. The designer of the system depends on rigorous definitions of goals and predefined targets to be able to implement and test the functionality of the system. This conversion of ideas into a computer-based, stringent reality may reveal information on what actually affects the brain and what does not, as observed in the feedback studies (PAPER 1 and STUDY 4).

I suggest that here the computer technology may play a very important role in treatment research. Each time computer training fails to achieve results, it is important to analyse why rather than dismiss technology as being the problem. Barring mundane programming errors, a failure basically indicates that the underlying model guiding the design of the training is not correct. My claim is also that the use of technology may be a way to challenge the brain in ways not ordinarily available to researchers in real life. In the studies of feedback (Wilms & Malá, 2010), the change in the presentation of feedback revealed that this might in fact have an impact on the visuomotor adaptation. Other studies seem to have observed similar effects but not attended to them. As mentioned earlier, in the study of the impact of delayed feedback, Tanaka et al (2011) mention only briefly that their initial experiment was done with a cursor position as feedback and that they switched to terminal exposure because the learning curves differed from those in other studies. Hopefully, they will pursue a reason for this difference in later study.

PAPER 3 in this thesis (Wilms & Mogensen, 2012) is an attempt to capture the dichotomy in the use of technology. On the one hand, technology is an excellent tool which, if used correctly, offers opportunities for better, cheaper and more pervasive assessment and training. On the other hand, the use of technology introduces more complexity and requires thorough understanding of the experience-based plasticity mechanisms to be activated through training to achieve long term and generalized effects. Converting standard training to a computer-based environment does not in itself add to the effectiveness of the solution. However, by paying close attention to the similarities and differences in response to training under different implementations, new and hitherto unknown or hidden aspects of a deficit and the underlying nature of recovery and compensation may be revealed.

The use of advanced technology in cognitive treatment deserves recognition as a research field of its own right in need of attention to the special challenges of cognitive experience-based rehabilitation.

## Chapter 6 - Artificial Intelligence and Rehabilitation

Following the general chapter on technology in rehabilitation treatment, this chapter focus on one particular technology, artificial intelligence (AI) and how it may be used to control a particular aspect important to experience-based plasticity - the progress of training. It positions the study in PAPER 2.

### Adjusting level of difficulty in cognitive rehabilitation

When training a patient, a skilled therapist is able to constantly monitor and modify the training activity to match the patient's mood, skills and learning rate. If a particular area seems difficult to master, the therapist can simplify the training, choose another approach or, postpone it until later. Constraint-induced language therapy is an example of this type of training (Meinzer et al., 2004; Pulvermuller, et al., 2001), where a small group of patients are playing a card game, which requires various forms of communication that can be adjusted by the therapist according to the skills and capability of the individual player. As the patients become more competent, they are required to use more sophisticated verbal skills in communication.

Moving up one step, the therapist can pre-plan a certain set of tasks that the patient need to accomplish in a predefined sequence. Usually progression from one task to the next is determined by a percentage of correct answers. Basic computer assistance can be introduced as in Mortley et al. (2001), where the computer is monitoring the patient's performance and providing the therapist with data necessary to determine how to progress. The tasks can also be pre-programmed by the therapist as in the "Afasi-assistant" system (Pedersen, Vinter, & Olsen, 2001), where the patient is guided by the computer through the pre-programmed set of computer-based training tasks, aimed at improving anomia step by step, based on a specific level of patient performance.

More automatic progression is accomplished by pre-programming (scripting) a set of paths which may be activated when reaching a pre-programmed level of competency as in computerized aphasia training (Katz & Nagy, 1984, 1985; Katz & Wertz, 1989; Wertz & Katz, 2004). Another example is the CogMed system aimed at improving short-term memory. Here, the user is progressing through levels of increasingly more difficult tasks, but is required to master one before advancing to the next. CogMed has the added feature that



difficulty may automatically regress, if the user repeatedly fails a task at a higher level (Klingberg, 2007; Lundqvist, Grundstrom, Samuelsson, & Ronnberg, 2010; Westerberg et al., 2007). A similar method of progression was administered in perimetry treatment of visual impairments (Schmielau & Wong, 2007).

Cueing is another way of increasing or reducing difficulty. By letting the patient get access to more or less assistive information during training, a task can become easier or harder without breaking the general progress of the patient. Examples are found in word mobilization, where the display of pictures of objects or written words may cue verbal pronunciation (Abel, Schultz, Radermacher, Willmes, & Huber, 2005; Breitenstein et al., 2007; Fink, Brecher, Sobel, & Schwartz, 2005; Katz & Nagy, 1984, 1985; Kim, et al., 2004; Ramsberger & Marie, 2007) or attention training where attention may be directed towards a particular item or spot using sound or light after a period of time (e.g. Myers & Bierig, 2000; Robertson, Mattingley, Rorden, & Driver, 1998).

A recent development within computerized assessment is to let the scores from one test be the input for selection of further tests in which testing parameters and elements are set to match the performance and skills of the individual patient (Donovan, et al., 2011; Gur, et al., 2010). Since computerized tests can be scored instantly, the scores themselves along with the detected characteristics of behaviour during assessment may be feed directly into the assessment system and serve as selection criteria for the next test to follow. The potential to feed these results into training systems which then tailor a plan based on the assessment scores may be a viable way for future research into technological advanced training.

Although the controls asserted above, at surface level, may be termed advanced control of the progression and delivery of training, most of them still only partially address the more fundamental challenges in the delivery of treatment - the diversity and uniqueness in the impact of brain injury and the fluctuating performance of the patient. The path to achieving a skill may vary considerably from patient to patient and computerized training needs to be flexible and modular since even small variations in training may influence difficulty for the individual patient. One approach to this challenge has been demonstrated in the study in PAPER 2. In this study, the question of difficulty was approached from a different angle using user modelling and artificial intelligence to determine and control difficulty and progression.

A fundamental set of parameters each controlled a particular aspect of difficulty. In combination the value of the parameters defined the continuum from easy to difficult based on the real-time characteristics of an individual patient. Artificial intelligence algorithms were used to monitor progress and adjust the value of each parameter accordingly to match the progress and state of the patient.

Furthermore, to verify the potentials of this approach a patient was subjected to three weeks of visual attention training in which difficulty was controlled by three parameters: number of items on the screen, length of a word displayed inside each item and finally the variety of letters used to compose the words. The AI engine controlling the parameters was fairly simple, but the result was a fairly complex set of combinations only possible to control using online assessment and adaptation of the parameters. The study demonstrated that the AI engine was able to construct a level of difficulty that challenged the patient and changed as the patient improved. In this study, the reaction time of the patient was fed into the algorithm as feedback, but from the perspective of the AI algorithms, it might as well have been error rate or galvanic skin response, EEG input or any type of feedback indicating treatment progress. Quantitative measurement that changes in response to training might be used as valid input to the AI algorithms as long as they fit within a set range of acceptable responses. Even this range may initially be calculated using the AI algorithms and in this manner, the use of AI would accommodate for the fact that learning and ability do not always follow a straight progressive line but may occur in jumps (Robertson & Murre, 1999) and even temporarily relapse (Wilms, 2011).

## Chapter 7 – Concluding comments

The use of computer technology in rehabilitation of patients with brain injury is not a new trend. Computer technology is used pervasively within all major aspects of cognitive rehabilitation research: Mapping, analysis, diagnostics and therapy. Data from brain scanners and EEG equipment are collected, converted, compressed and translated into graphical representations, making the complex material easier to interpret and act upon by humans. Similarly, results from training and assessment are being manipulated, compressed and modelled using advanced analysis and statistics able to convert data into numbers or graphs, easier to evaluate and interpret by humans. However, the use of technology in rehabilitation training is in my view still at a very basic level and does not utilize that computers are able to analyse and react to complex training data faster than the human therapist.

As the study in PAPER 2 demonstrates, it is possible to create adaptive computer-based training that constantly monitors the skill level of a patient and modulates the level of difficulty accordingly, by manipulating multidimensional difficulty parameters. Although a therapist may do the same after each training session, the computer is able to do this even from trial to trial during training. In the PAPER 2 study, response time was used as an indicator of progress, but, from a technological point of view, any indicator may be used as long as the indicator changes in response to training. By defining level of difficulty in relation to parameters, each representing an aspect of skill that might be impaired as a result of brain injury, the same computer-based training system is able to adapt training to the individual strengths and weaknesses of a patient. The adaptation is not just based in an initial model of the patient's ability but on the actual ability at any given time.

But it is not without problems to introduce advanced technology in such a diverse field as rehabilitation after brain injury. As the theoretical PAPER 3 and the studies in PAPER 1 and STUDY 4 imply, adding technology into the equation of therapy and training adds to the complexity of interpreting the experimental results. Seemingly similar training conditions conducted on computer or in session with a therapist may yield different results due to slight variations in the way the training is conducted. The use of advanced technology in itself does not improve skills or knowledge in humans. Only skilled and clever

implementations of training founded on theoretical and empirical knowledge stands a chance to succeed in the promotion of learning and rehabilitation. Even to this day, there seems to be a lack of appreciation that although the introduction of advanced technology will provide huge benefits, it also introduces further complexity and a new set of challenges to be dealt with.

On the other hand, the activity of trying to translate existing assessments and training into computer-based versions may very well reveal new and important knowledge about the brain and how circumstances influence experience-based plasticity.

Feedback is an important element in learning and adjustment, and the results from the studies in PAPER 1 and STUDY 4 indicate that the mechanisms of experience-based plasticity may react differently to the direct or indirect presentation of feedback. I have ventured into proposing the hypothesis that direct feedback require no cognitive control as opposed to indirect feedback and that this may account for the difference in adaptation. The results from the studies are not yet conclusive and further studies are required to understand how and why this difference occurs.

The studies presented in this thesis are linked together in the attempt to investigate how feedback may be used in the experience-based adaptation of both human and computer in close interaction. The studies emphasize that progress in rehabilitation training research depends on input from many different research disciplines as well as close interaction between basic research, applied clinical research and clinical practice.

## List of abbreviations

AI	Artificial Intelligence – the study and design of intelligent systems (agents) able to achieve goals through intelligent behaviour.
AS	Algorithmic Strategy – a combination of elementary functions needed to express a behaviour.
CRBI	Center for Rehabilitation of Brain Injury – a rehabilitation clinic and research unit for patients in need treatment after acquired brain injury. CRBI offers comprehensive cognitive and physical training programmes aimed at returning the patient to a more self-sustained life.
CVC	Center for Visual Cognition – a research unit at the Department of Psychology at the University of Copenhagen working with basic research in areas such as visual perception and attention.
EEG	Electroencephalography – recording of electrical activity in neurons in cortex through electrodes placed on the scalp.
fMRI	Functional Magnetic Resonance Imaging. An imaging technique which measures the change in blood flow and deoxygenation related to neural activity in the brain.
LED	Light-Emitting Diode – small light emitting electronic device with very low energy consumption.
NIRS	Near-infrared Spectroscopy - measures cerebral activity by function by monitoring the changes in emission of near-infrared waves from oxidative metabolism in cerebral tissue.
PAT	Prism Adaptation Therapy – a therapy for patients suffering from the impairment – neglect. The patient is exposed to prism-induced distortion of visual input during pointing activity.
PA	Prism Adaptation – the ability of the brain to adapt to visual input distortion from prism goggles.

REF            Reorganization of Elementary Functions – a model of the possible mechanisms behind recovery of function in rehabilitation.

## **Wordlist**

Brain injury            In this document, brain injury refers to injury sustained to a previously healthy brain through trauma, ischemia, thrombosis or haemorrhage.

Hypoperfusion            Restricted or reduced blood flow.

Neglect            An attention deficit characterized by an inability to respond to or orient towards objects in the contralesional space which cannot be attributed to visual impairments.

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## Co-authorship statements

Co-author statement regarding the publication:

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I hereby confirm that the above-mentioned publication is a collaborative project and that Inge Wilms has contributed significantly during all phases of the project.

Yours sincerely



Jesper Mogensen

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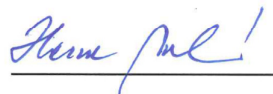
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The primary author formulated the scientific problem and designed the experiment in collaboration with the co-author. The primary author constructed the physical boxes used and programmed the training programs. She supervised and coordinated the testing of subjects with which she received assistance from the co-author. Statistical analysis, data interpretation, and manuscript preparation were the responsibilities of the primary author."

In Copenhagen, July 11<sup>th</sup>, 2011



Hana Malá, Co-author

## Papers

This section contains the three original research publications:

### PAPER 1:

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### PAPER 2:

Wilms, I. (2011): “Using Artificial Intelligence to Control and Adapt Level of Difficulty in Computer-Based, Cognitive Therapy – an Explorative Study”. *Journal of Cybertherapy and Rehabilitation*, vol. 4(3), 387-397.

### PAPER 3:

Wilms, I., Mogensen, J. (2012): “Dissimilar Outcomes of Apparently Similar Procedures as a Challenge to Clinical Neurorehabilitation and Basic Research - when the Same is not the Same”. *Neurorehabilitation*, accepted for publication in January 2012.





## Indirect versus direct feedback in computer-based Prism Adaptation Therapy

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Prism Adaptation Therapy (PAT) is an intervention method in the treatment of the attention disorder neglect (Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Rossetti et al., 1998). The aim of this study was to investigate whether one session of PAT using a computer-attached touchscreen would produce similar after-effects to the conventional box normally used in PAT.

In four experiments, 81 healthy subjects and 7 brain-injured patients diagnosed with neglect were subjected to a single session of PAT under two conditions: (1) using the original box, and (2) using a computer-based implementation of PAT. The session of PAT included a pre-exposure step involving pointing at 30 targets without feedback; an exposure step involving pointing at 90 targets with prism goggles and feedback; and a post-exposure step involving pointing at 60 targets, with no goggles and no feedback.

The results indicate that the expected similarity in the after-effect produced by the two conditions seems to occur only if subjects receive feedback on pointing precision by seeing their fingertip during the exposure step. Attempts to provide feedback indirectly via icons on the computer screen failed to produce the expected size in the after-effect. The findings have direct implications for computer-based treatment of visuospatial disorders in the future and computer-assisted rehabilitation in general.

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**Keywords:** Neglect; Prism Adaptation Therapy; Feedback; Computer-based therapy; Visuomotor plasticity.

## INTRODUCTION

Within the field of cognitive rehabilitation, the positive effects of intensive, focused training (Kleim & Jones, 2008; Meinzer et al., 2004; Pulvermüller & Berthier, 2008) has generated renewed interest in transferring paper-and-pencil therapy to a computer-based environment.

Many types of neuropsychological rehabilitation efforts are often conducted on a paper-and-pencil basis requiring the constant presence and supervision of a therapist. The transfer of paper-and-pencil therapy to a computer environment would provide choice and flexibility in access to training at rehabilitation clinics and at home. Furthermore, it would facilitate more detailed and precise recordings of information during training; allow adjustment of training according to individual progress; and potentially reduce therapist workload as the demands for intensity and frequency of therapy increases. Finally, the use of computer-based training in research would ensure that the training is delivered in a consistent manner, which makes comparisons across subjects more valid.

The usefulness of computers has been demonstrated with standard neuropsychological tests which, when transferred to computer, have been shown to improve the quality of observations and the level of detail available to therapists (Chiba, Yamaguchi, & Eto, 2006; Rabuffetti et al., 2002; Tsirlin, Dupierri, Chokron, Coquillart, & Ohlmann, 2009). Also, experimental use of computers in rehabilitation training has been successfully tested in various research settings (Ansuini, Pierno, Lusher, & Castiello, 2006; Katz et al., 2005; Kim et al., 2007; Smith, Hebert, & Reid, 2007; Turton, O'Leary, Gabb, Woodward, & Gilchrist, 2010; Webster et al., 2001). However, in both test situations and in therapy, it seldom seems to be a point of concern that the transfer of paper-and-pencil training to computer may introduce changes to the training, some beneficial and others detrimental.

As this study will demonstrate, an important aspect of transferring paper-and-pencil therapy into a computer-based environment is that this requires not only technical skills, but also detailed insights into which elements of the therapy are actually ameliorating the patient's symptoms as well as rigorous testing to ensure that the results obtained using one implementation of training are replicable with another, seemingly similar, method of implementation.

## Definition of key concepts

*Neglect.* One of the more common deficits after brain injury to the right hemisphere is hemispatial neglect (Rossetti et al., 1998). Hemispatial neglect is defined as a failure to explore, respond or orient towards stimuli presented on the contralesional side (Heilman, Valenstein, & Watson, 2000). Increasingly, evidence supports that some effects of unilateral neglect can be ameliorated by Prism Adaptation Therapy (Frassinetti et al., 2002; Rossetti et al., 1998; Serino, Bonifazi, Pierfederici, & Ladavas, 2007; Vangkilde & Habeck, in press). Other therapies also exist but are not relevant to this study.

*Prism Adaptation Therapy.* Prism Adaptation Therapy (PAT) is an intensive, bottom-up type therapy thought to affect visuospatial representations as well as visuomotor abilities (Frassinetti et al., 2002; Serino et al., 2007). A PAT session ordinarily consists of three steps; a pre-exposure step measuring the pointing accuracy of the patient without feedback or intervention; an exposure step where the patient must adapt to a rightward shift of the visual field induced by prism goggles; and finally a post-exposure step that measures the after-effect resulting from the exposure step. Each session is delivered twice a day for 2 weeks. During each step of a session of ordinary PAT, the patient is directed to point to one of several targets at the far end of a box placed between the patient and the therapist. The box is wide enough to allow almost full extension of the arm but constructed to hide the patient's arm and hand movements. The position of the box is adjusted during training to allow or prevent the patient from seeing the fingertip. For more details on PAT, see Serino et al., 2007.

*The after-effect.* Normally, patients as well as healthy controls are able to adapt to the rightward shift induced by the prism goggles after a certain number of attempts at pointing at targets, when provided with feedback about the precision of their pointing in relation to the specific targets (Frassinetti et al., 2002; Redding, Rossetti, & Wallace, 2005; Sarri et al., 2008; Serino, Angeli, Frassinetti, & Ladavas, 2006; Serino et al., 2007). After removal of the prism goggles a brief after-effect of off-target pointing to the left can be observed (Fernández-Ruiz & Díaz, 1999; Redding et al., 2005). The size of the after-effect, produced as a result of exposure to prism goggles, has been shown to be affected by whether or not the subjects are allowed to see the actual movement of the extremity during prism exposure (Redding et al., 2005; Redding & Wallace, 1988) on the task performed (Simani, McGuire, & Sabes, 2007), and may even be the additive result of the adaptation of different mechanisms (Redding & Wallace, 2002).

## Aim of the study

In the present study, we wanted to investigate if PAT could be successfully transferred to a computer-based environment. There are several reasons for this choice. Firstly, PAT is a fairly simple and repetitive type of training with well-defined rules, which lends itself to computer implementation. Secondly, some elements of the therapy, such as the observed adaptation effect and after-effect, can be measured in a non-injured population (Bedford, 1993; Fernández-Ruiz & Díaz, 1999; Redding et al., 2005) thus increasing the number of tested subjects and the statistical validity of the findings. Thirdly, using a non-injured population prevents contamination of the initial results from unknown effects of the brain injury itself.

Transferring therapy from one setting to another requires detailed study to ensure that the elements of therapy that make a difference are conserved across settings. In order to investigate whether a transfer of Prism Adaption Therapy to computer affected the effectiveness of the therapy, four experiments were carried out with the following aims:

1. To investigate whether the execution of a PAT session in a computer-based environment leads to similar after-effects in healthy subjects as a PAT session conducted in a standard box for each individual tested.
2. To examine whether the use of prism goggles could be replaced by displaced feedback on a computer touchscreen in healthy subjects.
3. To study the visuomotor elements characterising PAT.
4. Finally, assuming that both conditions would provide similar responses in after-effect during post-exposure in healthy subjects, we wanted to test if similar results could be obtained with brain-injured patients.

## METHOD

In our study, all participants in the four experiments performed a single session of PAT on both the box normally used in standard PAT and on a computer-based condition of PAT. The after-effect data from the single session on the box set the standard by which the subjects' responses in the computer-based conditions were compared. Data on pointing precision were recorded on computer or by a therapist.

A single session of PAT in our experiments consisted of three different steps of pointing at targets under different conditions:

1. A pre-exposure step, which served as a baseline for each individual tested. This step consisted of 30 pointing trials.

2. An exposure step, in which the subjects were exposed to prism goggles that shift the visual field 10 degrees to the right. This step consisted of 90 pointing trials.
3. A post-exposure step similar to the pre-exposure step to measure the after-effect of adapting to prism goggles. This step consisted of 60 pointing trials.

In all four experiments, the participants were instructed to execute the arm movement at the same speed, as if reaching for a glass of water, and to position the pointing hand above the sternum after each pointing trial. The recommended speed was based on the experimenters' own observations of what speed was appropriate to prevent corrections when the tip of the finger became visible. If necessary, patients were reminded to keep up the speed during testing.

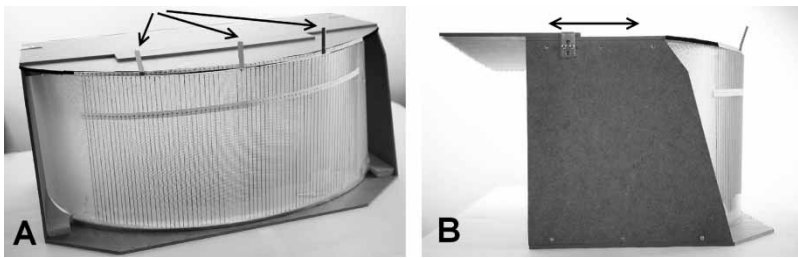
## Measures

The most important measure of similarity between the box and the computer conditions were the after-effects within subjects. For each pointing task, a relative deviation from target was calculated as the ideal position minus actual position in degrees. These deviations were used to calculate the mean deviation for each of the three pointing positions in each method and finally the mean for each step.

In these experiments, terminal exposure (seeing only the tip of the finger in the exposure step) was chosen as opposed to concurrent exposure (full view of arm movement during target pointing in the exposure step). It has been demonstrated that the adaptive processes are influenced by the choice of feedback (Redding et al., 2005; Redding & Wallace, 1988). However, this was initially considered not to be a concern as the total sum of effect is the same for both types of feedback. The use of terminal exposure was needed to record changes in pointing errors per trial during the exposure step which would be used to determine if the learning curves were similar for the conditions being tested.

## Equipment and procedures

*The box setup.* The box (Figure 1) was designed according to the specifications from Frassenetti et al.'s study (2002). Three targets were visible at all times at positions  $-21$ ,  $0$  and  $+21$  degrees (see Figure 1). In all three steps, trials were distributed equally among the three targets. Subjects would receive feedback on pointing precision in the exposure step by being allowed to see the tip of their finger. To prevent confounding of the after-effect, the subjects were asked to keep the prism goggles on until the very moment the post-exposure step started.



**Figure 1.** (A) The box used for standard PAT viewed from the experimenter end with the three targets in different colours on top (indicated by the arrows). (B) The opaque barrier was added in Experiment 2. Note that the top can slide back and forth to adjust it to the individual arm length of the subjects.

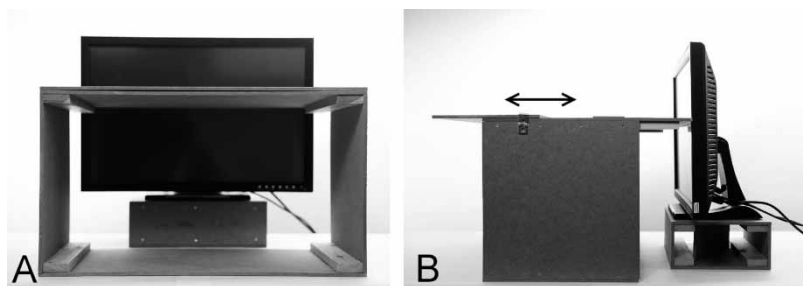
During all three steps, an experimenter orally indicated the target positions by stating the colour of the target. After each pointing task, the experimenter recorded the resulting pointing position in degrees.

In Experiments 2, 3 and 4, a barrier of opaque plastic was inserted into the target end of the box. The purpose of the barrier was to simulate the tactile sensation experienced when hitting the touchscreen during the pointing tasks, thus evening out any potential differences in feedback between the two conditions. The barrier itself was not visible to the test subjects.

*The computer-based setup.* The computer-based setup consisted of a PC, a touchscreen, a specially constructed wooden screen and prism goggles. The PC was a standard PC with Windows XP and JAVA installed. The attached monitor was a 22-inch touch-sensitive TFT LCD monitor (DT220TSR5U) with a response time  $\leq 5$  ms. The touch technology was a 5-wire, analogue resistive type with a touch resolution of 4096 x 4096 and a screen resolution of 1680 x 1050 pixels with a refresh rate of 75 Hz.

The software programs used in the computer conditions were developed by one of the authors (Inge Wilms) to follow the same protocol as the box condition, i.e., one session of PAT with three steps. The display on the touchscreen was divided into two parts. On the upper part, the program would display a pointing target similar in size and shape to those in the box condition. The lower part was constructed as a large touch-button in Java. Targets appeared at one of three different positions in the upper part of the touchscreen along the same horizontal axis in a pseudo-random order controlled by an algorithm ensuring that each target was presented an equal number of times. The target would remain visible until the subject had responded. The program recorded detailed information regarding accuracy of the subjects' pointing position throughout the session.

Only the top part of the touchscreen was visible to the subjects as a specially constructed wooden screen was placed in front of the touchscreen



**Figure 2.** The equipment used in the computer conditions. (A) Touchscreen and the wooden screen that hides the arm movements. The wooden screen divides the touchscreen into two parts. The bottom part is where the subjects point and the top part is where the targets are shown. (B) Note that the top can slide on the wooden screen to adjust for the arm length of the subjects (indicated by the double headed arrow).

to prevent the subjects from seeing their arm movements (see Figure 2) and the touch area. The screen had a sliding top that was adjusted to the subjects' arm length. The touchscreen issued a beeping sound when touched, indicating to the subject that the pointing was recorded. The program ignored any accidental repeated touches.

*Prism goggles.* The prism goggles in this study were constructed using a standard pair of goggles with large viewing area lined with Fresnel prisms of 17.5 dioptre, which shifted the visual field 10 degrees to the right. Initially, when wearing the prism goggles, subjects will tend to point too far to the right of the targets because of the deviation of the visual field. Gradually during the exposure step, subjects will adapt to the change and the pointing measurements settle around the target.

*Finger nail.* During all trials, the subjects wore a 3mm broad plastic nail on the pointing finger to prevent direct tactile feedback upon touching the screen or box. The plastic nail was attached with adhesive tape to the finger to prevent bending and sliding and extended the physical nail by approx. 5mm.

*Statistics.* SPSS version 17.0 was used to analyse the data. Kolgorov-Smirnoff tests were used to test normality and MANOVA and ANOVA tests were used to test variance and means. *T*-tests were employed to isolate group differences where group differences had been demonstrated with the ANOVA and MANOVA tests.

EXPERIMENTS

A total of four experiments were carried out to gather data under the computer condition. Before the actual sessions, each participant was allowed five practice trials on the computer and the box to become familiar with the movement requirements and the touchscreen. The data from these trials were discarded from the analysis.

Each experiment is described in detail in the following paragraphs along with results. Table 1 provides an overview of the different conditions for each experiment.

TABLE 1  
Overview of the experimental conditions for the four experiments.

	<i>Type of Feedback</i>	<i>Artificial Nail</i>	<i>Pointing instr.</i>	<i>No. of targets visible</i>	<i>Barrier on box</i>	<i>Distance between targets</i>	<i>No. of test subjects</i>	<i>Type of subject</i>
<b>Experiment 1 conditions</b>								
Computer A, goggles	X on screen	Yes	SVT	1		14 cm	33	Normal
Computer B, no goggles	X on screen	Yes	SVT	1		14 cm	33	Normal
Box	Visible finger	Yes	OI	3	no	17.5 cm	33	Normal
<b>Experiment 2 conditions</b>								
Computer A, goggles	Visible finger	Yes	SVT	1		14 cm	28	Normal
Box	Visible finger	Yes	OI	3	yes	17.5 cm	28	Normal
<b>Experiment 3 conditions</b>								
Computer A, goggles	Visible finger	Yes	OI	3		14 cm	20	Normal
Box	Visible finger	Yes	OI	3	yes	14 cm	20	Normal
<b>Experiment 4 condition</b>								
Computer A, goggles	Visible finger	Yes	SVT	1		14 cm	7	Brain injured
Box	Visible finger	Yes	OI	3	yes	17.5 cm	7	Brain injured

SVT denotes that a single target was visible at a time on the touchscreen as opposed to the three permanently visible targets in the box condition. OI (oral instruction) indicates that instruction on current target was given orally.



## Experiment 1

In the first experiment, we wanted to test if the after-effect observed after a single session of PAT in the box condition was reproducible with two different computer conditions.

The computer condition “A” was designed to emulate the three steps of a single standard session of PAT in the box. Due to the limited width of the touchscreen, the distance between targets were slightly shorter (by 3.5cm) on the touchscreen as compared to the box. We compensated for this by placing the subjects 9cm closer to the touchscreen, so the visual angle was constant across conditions.

The subjects were instructed to imagine that the displayed target on the touchscreen extended downwards below the edge of the wooden screen hiding their movement and finger (see Figure 2A) and that their objective was to hit the extended target as precisely as possible. A red “X” was displayed on the touchscreen above the barrier as indirect feedback on the horizontal precision of the pointing position in the exposure step. Subjects were told to try to position the red “X” exactly on top of the target.

In computer condition “B”, the setup was similar to the “A” condition except for the exposure step. In the “B” condition, subjects were not asked to wear prism goggles but instead received displaced feedback on pointing precision. The displacement equalled a rightward shift of 10 degrees similar to the effect of wearing prism goggles. The rationale was that by providing displaced feedback the subjects would be forced to adjust eye-to-hand coordination without the use of prism goggles.

A total of 33 healthy subjects completed three sessions of PAT, one on each of the three conditions: box, computer “A”, and computer “B”. Since all three conditions were very similar, each subject was exposed to only one condition a week to reduce the effect of repetition inadvertently confounding the results. Furthermore, the subjects were randomly assigned to six groups, each trying out the conditions in six different predefined sequences to avoid any sequencing effect. The six sequence-groups were the following with “A” and “B” being the computer conditions and “box” being the box: “A, B, box”; “A, box, B”; “B, A, box”; “B, box, A”; “box, A, B” and “box, B, A”.

### *Participants*

Thirty-three subjects participated in this experiment. The age of the subjects ranged from 26 to 59 ( $M = 38.48$ ,  $SD = 9.38$ ,  $n = 33$ ), 27 females and 6 males. The participants were recruited from the employees at the Center for Rehabilitation of Brain Injury (CRBI), University of Copenhagen, Denmark.

## Results

Data were tested for normality using the Kolmogorov-Smirnov test and no significant deviation from normality was found at the pre-exposure and post-exposure step. A slight deviation was observed in the data from the exposure step (K-S,  $p < 16.2$ ) for the box condition. Since the main parameter for measuring the similarity in effect was the after-effect in the post-exposure step, parametric statistical models were used to analyse the similarities and differences.

To determine if the conditions produced similar after-effects, the general linear model for repeated measures to analyse variance was used to test the conditions within subjects. It showed a highly significant difference between conditions per step,  $F(4, 128) = 9.223$ ,  $p < .001$ . A Mauchly's test of sphericity on conditions per step was significant ( $p < .003$ ). As such, the more conservative Greenhouse-Geisser and the Huynh-Feldt corrections were used as recommended by Field (2009) both of which confirmed the significant difference, G-G,  $F(2.99, 95.91) = 9.223$ ,  $p < .001$ ; and H-F,  $F(3.34, 106.92) = 9.223$ ,  $p < .001$ .

To isolate the group difference, a paired sample *T*-test was performed on the three pairs of conditions ("A"-box, "B"-box, "A"- "B"). The mean diversion for the box condition ( $M = 4.17$ ,  $SD = 1.96$ ) and the computer "A" condition ( $M = 2.01$ ,  $SD = 1.61$ ) was significantly different ( $t = 5.68$ ,  $df = 32$ ,  $p < .001$ ); likewise with the paired samples *T*-test between diversion from the box condition and the computer "B" condition ( $M = 2.25$ ,  $SD = 1.99$ ). They were also significantly different ( $t = 3.92$ ,  $df = 32$ ,  $p < .001$ ). Finally, means from the after-effect measured for the two computer conditions were compared. They were not significantly different ( $t = -0.74$ ,  $df = 32$ ,  $p < .47$ ).

In summary, the analysis showed that the after-effect following the standard box setup was different from the one achieved on the two computerised versions of the experiment. No significant impact on the after-effect was found from age, sex and the six different sequences.

## Discussion

The results from the single session of PAT conducted on the computer conditions "A" and "B" showed the same amplitude in the after-effect. However, both computer conditions differed significantly in the amplitude of the after-effect from the box condition. By far the largest amplitude was measured for the box with a mean 2 degrees larger than the computer conditions. Seeing something about the computer conditions was causing lower amplitude in the after-effect. The fact that both computer conditions elicited similar results suggested further investigation into the major differences between the

computer conditions and the box condition. The following differences were identified:

1. Only a single target was shown on the touchscreen at a time as opposed to three visible targets on top of the box.
2. Feedback was in the shape of an “X” on the touchscreen as opposed to the fingertip viewed in the box condition.
3. Distance between target position was slightly smaller on the touchscreen than in the box condition.
4. When pointing at the touchscreen, the fingertip would hit a solid surface as opposed to the box where subjects would point into open space.
5. The target was indicated by vocal instruction in the box condition versus implicit positioning of only one target in the computer conditions.

The most prominent difference between the computer conditions and the box condition was the difference in the presentation of feedback on pointing precision. We hypothesised that the indirect feedback did not activate the eye-to-hand coordination system adequately even though subjects solved the pointing tasks correctly during all three steps and were explicitly aware that the “X” on the touchscreen was the feedback on pointing position. Another interesting finding was that goggles and indirect feedback from the “A” condition created the same after-effect size as the displaced feedback with goggles.

## Experiment 2

Based on the results from Experiment 1, we hypothesised that it may be essential to receive feedback by viewing one’s own fingertip, and discarded the “B” condition, as any visual feedback would reveal that it was artificially skewed by 10 degrees. Therefore in Experiment 2, only a modified version of the “A” condition was tested against the box condition. The indirect “X” feedback was replaced by direct fingertip feedback by moving the wooden screen slightly away from the touchscreen in the exposure step.

In addition, the box used in Experiment 1 was modified by inserting an opaque barrier invisible to the subjects at the back end (see Figure 1B). The intention was to mimic the tactile feedback from the touchscreen, thus eliminating any impact this might have on the results. This change also eased recording of the pointing position by the experimenter and prevented accidental exposure of the finger in the post-exposure step (a potential confounder detected in the first experiment).

As in Experiment 1, only one target was shown at a time on the touchscreen thus implicitly indicating where to point. The pointing regime was similar to the one used in Experiment 1.

The subjects were randomly divided into two groups, one starting with the session on the box and the other starting with the computer condition to prevent any effects from the test sequence.

### *Participants*

A total of 28 healthy subjects were tested with the standard PAT and on the computer. The age of the subjects ranged between 20 and 48 ( $M = 26.821$ ,  $SD = 7.68$ ,  $n = 28$ ), 23 females and 5 males. They were all recruited from the employees and student population at the Department of Psychology, University of Copenhagen, Denmark.

### *Results*

Data were tested for normality using the Kolmogorov-Smirnov test and no significant deviation from normality was found at the pre-exposure and post-exposure steps but a significant deviation was found in the exposure step ( $K-S$ ,  $p < .001$ ) for both conditions.

To compare the two conditions within subjects, we tested variance using the general linear model for repeated measures within subject. The result showed no significant difference between the conditions,  $F(1, 27) = 0.021$ ,  $p = .885$ , in the after-effect for the box ( $M = 4.90$ ,  $SD = 2.07$ ) and the computer-based condition ( $M = 4.95$ ,  $SD = 2.15$ ).

Two changes were made from Experiment 1 to Experiment 2: the addition of the opaque barrier and the change to direct feedback on the computer. To test whether the barrier change made any difference, the results from the box condition in Experiment 1 were compared to the results from the box condition in Experiment 2 in an unrelated ANOVA test. The one-way ANOVA was chosen because the subjects differed in the two experiments. The result indicated that adding the barrier was insignificant,  $F(1, 59) = 0.598$ ,  $p = .443$ . To test for effect of the change in fingertip visibility, data from the computer condition "A" from Experiment 1 were compared to data from the computer conditions in Experiment 2. This comparison revealed a highly significant difference,  $F(1, 59) = 15.969$ ,  $p < .001$ , indicating that changing from indirect feedback to direct feedback (seeing one's own finger) was responsible for the change observed in the measured after-effect. In addition, possible effects of age, sex and condition method sequence were tested but, as in Experiment 1, there was no significant impact on the after-effect from any of the three.

### *Discussion*

The results from Experiment 2 showed that the amplitude in the after-effect created by the exercise on the computer condition now matched the

amplitude from the box condition results. As there was no change in the after-effect measured using the box in Experiments 1 and 2, the added barrier was ruled out as being the cause of the change. In other words, it was not the tactile sensation of hitting a barrier or touchscreen that changed the amplitude of the after-effect. Neither was it the potentially more precise recordings of pointing position due to the barrier.

The subject population was different for Experiments 1 and 2 and this changed the average age. If this had been responsible for the difference observed, one would have expected data from the box condition to also change between Experiments 1 and 2. As this was not observed, we concluded that the change in population did not influence the results.

The most probable cause of the impact on the after-effect was the change from providing indirect feedback about pointing precision using an "X" on the touchscreen to letting the subject see his/her own fingertip (with the artificial nail) in the computer condition. In conclusion, the results from Experiment 2 indicate that wearing prism goggles, doing the arm movements and solving the task of pointing increasingly precisely during the exposure step, does not in itself produce the desired amplitude of the after-effect. In other words being able to relate feedback to the bodily act of pointing by seeing one's actual fingertip is apparently also required.

### Experiment 3

Experiment 2 tested the significance of the barrier and visible feedback. In Experiment 3, the remainder of the differences detected from Experiment 1 between the computer condition and the box condition were tested. The data were used to analyse the effect of all of the observed differences between the computer and the standard box condition.

The box condition was modified so in addition to the added barrier, the distance between targets was changed to match the distance between targets on the touchscreen. Due to the limitation in the touchscreen size, i.e., 22 inches diagonal, the distance between targets on the touchscreen was 14cm as opposed to 17.5cm in the box condition in the previous experiments. Although subjects were placed closer to the screen, it was a potential confound and, therefore, in Experiment 3 the distance between the targets in the box was changed to match those on the touchscreen.

The computer-based condition was changed to match the box condition as closely as possible. All three targets were made visible at all times and coloured to match the targets in the box. A recorded voice would state which target to point at, simulating the voice of the experimenter. The subjects received direct feedback in the exposure step by actually seeing their own finger.

The subjects were randomly assigned to two groups, one starting with the box condition and one starting with the computer condition to avoid effects from the test sequence.

### *Participants*

Twenty normal subjects were tested in both conditions at least one week apart using one session of PAT. The age of the subjects ranged from 26 to 55 ( $M = 37.9$ ,  $SD = 10.6$ ,  $n = 20$ ), 17 females and 3 males. They were recruited from the student population at the Department of Psychology at the University of Copenhagen and among the employees at the Center for Rehabilitation of Brain Injury (CRBI).

### *Results*

Again data were tested for normality using a Kolmogorov-Smirnov test and no significant deviation from normality was found at any of the steps (K-S,  $p > .05$ ) for either condition.

To compare the two conditions within subjects, we tested variance using the general linear model for repeated measures. The results from the ANOVA showed no significant difference between the conditions,  $F(1, 19) = 1.776$ ,  $p = .198$ , for the after-effect.

A paired samples  $t$ -test of the means showed that the means for the box condition in the post step ( $M = 4.58$ ,  $SD = 2.176$ ) did not differ significantly from the means from the computer condition ( $M = 5.32$ ,  $SD = 2.50$ ) ( $t = 1.33$ ,  $df = 19$ ,  $p = .20$ ). This supports the hypothesis that the two conditions elicited the same results. In addition, we tested for the effect of age, sex and condition sequence and, as in Experiment 1, there was no significant impact on the after-effect from any of the three.

To test whether the changes made in Experiment 3 to the box changed the observed after-effects, we performed a one-way unrelated ANOVA between the results from the box condition in Experiments 1, 2 and 3. None of the changes seems to have made a significant change to the subjects' behaviour in relation to the box,  $F(2, 78) = 0.311$ ,  $p = .733$ . The means of the after-effect from the three experiments were 4.457, 4.900 and 4.578 and standard variation 2.323, 2.071, and 2.176 confirming that they were very much alike.

To check if the changes made to the computer condition in Experiment 3 in any way changed the behaviour of the subjects with regard to the after-effect, we compared the results from Experiments 2 and 3. No significant difference between the two versions of the computer condition in Experiments 2 and 3 were found,  $F(1, 46) = 0.304$ ,  $p = .584$ . This indicates that the changes made from Experiments 2 to 3 did not alter the performance of the subjects in any significant way.

### *Discussion*

In Experiment 3, the distance between targets in the box was changed to match the distance on the touchscreen. The computer condition was changed to show all three targets simultaneously as in the box condition. A recorded voice instructed the subjects to point to a specific target. The statistical tests support the assumption that none of these changes made any impact on the after-effect observed. Since observations from post-exposure in the box condition in this experiment matches the findings from the box condition in Experiment 1, we conclude that it is highly unlikely that any changes made in Experiment 3 had an effect on the after-effect.

This supports the findings from Experiment 2 that receiving direct feedback regarding pointing precision was the key to the difference in the observed after-effect.

### **Experiment 4**

A main motivator for this project was to find out if PAT for patients with neglect could be executed effectively on a computer in the hope that this would allow more people to train in clinics and at home. Therefore, in Experiment 4, we used the same procedure as for Experiment 2, only this time the two conditions were tested on seven subjects with acquired brain injury to the right cerebral hemisphere who had previously been diagnosed with unilateral neglect.

The subjects were randomly divided into two groups, one starting with the box condition and one starting with the computer condition to avoid effects from the test sequence. The sessions were separated by at least one week to diminish any unwarranted learning effect.

### *Participants*

Seven patients from the CRBI participated in this experiment (see Table 2 for details on impairment). All patients were in the chronic phase of recovery ( $> 6$  months post-injury) and all had been referred to CRBI with neglect-like symptoms in various degrees. In our experience neglect symptoms are much harder to detect using standard neuropsychological tests when patients are tested later than 6 months post-onset, partly due to interference from learned compensatory techniques. However, all subjects were retested for neglect using the Schenkenberg Line Bisection Task (Schenkenberg, Bradford, & Ajax, 1980), the Star and Letter Cancellation tasks (Weintraub, 2000), the Baking Tray Task (Appelros, Karlsson, Is, Tham, & Nydevik, 2004; Tham & Tegner, 1996) and the visual field and neglect test from the TAP (Testatterie zur Aufmerksamkeitsprüfung) battery (Zimmermann & Fimm, 2002). The age of the subjects ranged from 46 to 61 ( $M = 54.9$ ,

TABLE 2  
List of subjects and their aetiology

<i>Case</i>	<i>Age</i>	<i>Sex</i>	<i>Months post onset</i>	<i>Aetiology</i>	<i>Locus</i>	<i>Hemianopia</i>	<i>Hemiparesis</i>	<i>Neglect</i>
CH	59	M	12	Infarct	Right hemisphere		Y	N
LD	50	F	6	Haemorrhage	Basal ganglia, occipital/parietal lobe	Y		(Y)
LT	56	M	6	Haemorrhage	Right temporal/parietal lobe	Y		N
NT	61	M	25	Infarct	Right temporal lobe		Y	N
SA	46	F	20	Haemorrhage, hydrocephalus, meningitis	Right hemisphere	Y	Y	(Y)
SH	56	M	27	Fracture Comotio cerebrii	Right hemisphere			Y
SS	56	M	26	Infarct	Right hemisphere			Y

The information on pathology and locus have been copied directly from the original medical journals and although not as detailed as we would have wished, they are the best available. The "Neglect" column indicates the results from our tests. Parentheses indicate that results were ambiguous.

$SD = 9.31, n = 7$ ), two females and five males. All participants were given a thorough introduction to the project and care was taken to ensure that each clearly understood the purpose and the instructions provided. Each participant then signed a letter of consent.

Results

Data were first tested for normality using a Kolmogorov-Smirnov test and no significant deviation from normality was found at any of the steps ( $K-S, p > .05$ ) for either condition.

To compare the two conditions within subjects, variance was tested using the general linear model for repeated measures. The result from the ANOVA showed no significant difference between the conditions,  $F(1, 6) = 0.805, p = .404$ , for the after-effect.

A paired samples  $t$ -test of the means showed that the mean difference in degrees for the box condition in the post-exposure step ( $M = 4.93, SD = 1.36$ ) did not differ significantly from the means from the computer condition ( $M = 6.01, SD = 3.27$ ) ( $t = 0.897, df = 6, p = .404$ ). This



supports the hypothesis that they generate similar effects. Possible effects of age, sex and condition method sequence were tested using ANOVA and no significant impact on the after-effect from any of the three variables was observed.

In summary, the patient group showed effects of both standard and computerised PAT similar in magnitude to that found with normal subjects in the previous experiments.

Discussion

The results from Experiment 4 showed no significant difference in the magnitude of after-effect within subjects between the box and the computer conditions in the brain-injured patients. These results confirmed our findings from Experiment 2 with healthy subjects.

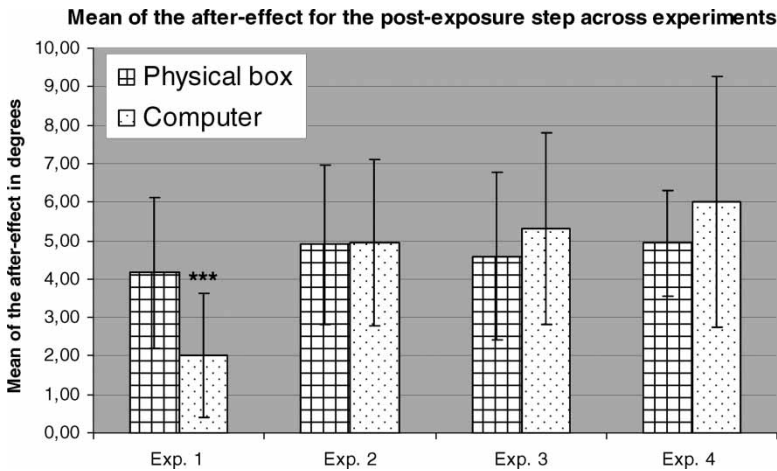
The primary reason for trying the conditions on the brain-injured population was to examine whether brain injury in itself influences the observed after-effect on either condition. Our data show no indication of this. Either one of the two conditions can, therefore, be applied in rehabilitation of brain injury with expected similar effects.

SUMMARY OF RESULTS FROM ALL FOUR EXPERIMENTS

In the four experiments, we showed that the amplitude of the after-effect was dependent on the type of feedback received during the exposure step. When subjects saw their own fingertip as feedback (direct feedback) on their pointing position during the exposure step, the after-effect was twice as large as when they received only indirect feedback (in the shape of an “X” on a computer touchscreen). See Table 3, which summarises the means and standard deviations for the after-effect measured during the four experiments, and Figure 3, which illustrates the observed after-effects from the four different experiments.

TABLE 3  
A summary of findings for the after-effect in degrees across experiments

	<i>Box mean (degree)</i>	<i>Box SD</i>	<i>Computer mean (degree)</i>	<i>Computer SD</i>	<i>n</i>
Exp. 1	4.17	1.96	2.01	1.61	33
Exp. 2	4.90	2.07	4.95	2.15	28
Exp. 3	4.58	2.18	5.32	2.5	20
Exp. 4	4.93	1.36	6.01	3.27	7



**Figure 3.** The resulting means of the after-effects in degrees from the post-exposure steps across experiments. \*\*\* Notice the significant difference in means in Experiment 1 ( $t = 5.68$ ,  $df = 32$ ,  $p > .001$ ).

## GENERAL DISCUSSION

Prism adaptation has been used in many studies to investigate how the brain learns and adapts to changes in the sensorimotor systems (e.g., Bedford, 1993; Clower & Boussaoud, 2000; Fernández-Ruiz & Díaz, 1999; Hatada, Miall, & Rossetti, 2006; Redding et al., 2005; Redding & Wallace, 1988; Rogers, Smith, & Schenk, 2009; Simani et al., 2007). The mechanisms involved in prism adaptation seem to involve recalibration between visual perception and the action-motor system as well as proprioceptive adaptation (Redding & Wallace, 2002) and may be influenced by the way feedback on action is provided (Redding & Wallace, 1988) and the type of feedback, either actual (direct) or representational (indirect) (Clower & Boussaoud, 2000).

The after-effect has also been shown to depend upon the amount of interaction between the visual and motor system during the exposure step, rather than the amount of time wearing prism goggles per se (Prablanc et al., 1975 cited by Fernández Ruiz & Díaz, 1999). Our study supports this finding: In all four experiments, the time spent on the exposure step in the box condition was longer due to the additional time spent by the experimenter recording pointing positions on a piece of paper and vocally indicating the next pointing position. However, the actual amount of eye-to-hand activity, i.e., 90 pointing tasks, were the same for both box and computer conditions. In Experiments 2, 3 and 4, we recorded the same amplitude in after-effect regardless of the difference in time spent wearing prism goggles.

Our experiments identify actual visual feedback as an important element in the amplitude size of the after-effect during visuomotor activity. This confirms the study by Clower and Boussaoud (2000). However, in our study the feedback was not provided in a delayed fashion but appeared immediately upon touch; all trials were conducted in normal daylight with full body and head movements allowed, and targets were visible until feedback had been provided. The difference in after-effect between direct and indirect feedback in our study was not as large as in Clower and Boussaoud. Further experiments are needed to determine if other types of indirect feedback would work.

Apparently, performing the actual movement and receiving feedback is not in itself enough to produce the after-effect. The manner in which feedback is provided also plays a crucial role. In our study, seeing the position of the finger in relation to the appointed target created larger after-effects.

With the pervasive use of advanced tools such as computers, it is surprising that, in order to produce changes in eye-to-hand coordination processes, one must see the finger itself. As our experiments indicate, performing the movements and receiving indirect feedback on a touchscreen was not enough. Yet, in many computer-related activities we are able to manipulate objects on the screen using an extension of our hand, such as the computer mouse, keyboard and game consoles. The activity on the screen in our experiments was very simple. All the subjects were consciously aware that the indirect feedback on the touchscreen was indeed feedback on pointing precision and all were able to adjust their pointing strategy during the exposure step. Furthermore, all subjects had previous computer experience and were accustomed to coordinating actions on computer screens using indirect pointing devices such as a computer mouse. Although the adaptation to the displaced visual input happened regardless of the type of feedback, the after-effect was highly susceptible to the type of feedback provided. We therefore conclude that although the executing element of the visuomotor system adapts to the changed input, allowing subjects to point at targets during the exposure step, other aspects of adaptation such as the impact depend on the type of feedback received.

## Feedback

Neglect can manifest itself in three distinct areas: body space, peripersonal space and extrapersonal space (Gamberini, Seraglia, & Priftis, 2008). In other words, neglect can be observed when dealing with objects out of reach and within reach. Gamberini et al. (2008) carried out a study with the line bisection test executed under two different conditions in extrapersonal space. In the first condition, a laser-pointer was used to bisect a line on a remotely placed computer screen; in the second condition, subjects wore a

glove and pointed with an actual stick into a virtual reality environment, which provided the user with tactile and proprioceptive feedback. The results showed that the stick was perceived as part of the peripersonal space whereas the laser pointer was not. Gamberini et al. suggested that the result was due to a remapping of peripersonal space and extrapersonal space. The results from our study may support another interpretation based on feedback rather than spaces. Bisecting a line with a laser-pointer (indirect) versus bisecting a line with a simulated extension of the body (direct) correlates with our findings where *seeing* one's own finger as feedback (direct) influences the visuomotor programming whereas seeing an "X" on a screen (indirect) does not. Our point is that both the finger and the "X" are within the peripersonal space so it is not as much the distance to the target but rather *how* feedback relates to the proprioceptive sense of body. If feedback is interpreted as coming from an action involving the body or an extension of the body, feedback will strengthen the impact (in our case the after-effect).

In Experiment 1, we also tested if displaced feedback on the touchscreen would elicit similar after-effects to those observed in the box condition. As it turned out, the after-effect produced by displaced feedback was not similar to the after-effect from direct feedback. The displaced feedback condition produced an after-effect similar to the indirect feedback condition.

Within the field of psychology, any type of training or therapy involving almost any type of computer interaction is commonly referred to as virtual reality (VR). The term is usually used more restrictively within the IT community to refer to humans navigating in a virtual 3D-world with interactive equipment such as helmet, gloves, etc., that creates an illusion of total immersion into the virtual world. There are studies that have looked at replacing the prism goggles with displaced or incongruent feedback in a virtual reality environment (Castiello, Lusher, Burton, Glover, & Disler, 2004; Glover & Castiello, 2006). The results show that it is possible to improve the coding of visual stimuli in the neglected field using displaced feedback. In our study we found that displaced feedback provided as an "X" on the touchscreen did not result in after-effects similar to the training in the box condition. A possible explanation is that in Castiello et al.'s (2004) experiments the level of immersion was greater than in ours. Subjects wore a haptic glove, which made it possible to "feel" the targets, and, on the screen, a virtual hand moved similarly to the actual physical movements. We speculate that the difference between our results from displaced feedback and those of Castiello et al. may be that in the virtual reality simulation, the visuomotor systems are adapting because feedback is perceived as directly related to a body part (the hand) whereas in our study, the "X" on the screen was not perceived as being part of the body even though subjects were never in doubt that it was feedback on the action of pointing.

In our view, this raises an important question concerning the use of computers in rehabilitation tests and therapy. Our results suggest that it is not enough to be consciously aware of the purpose of a task and even executing it correctly for therapy to have the wanted effect. In the case of visuomotor adaptation, the actions must be perceived as relating to the proprioceptive sense. Further research is needed to establish what exactly is needed for the proprioceptive system to respond to the feedback. Will a picture of a finger rather than the “X” on the screen be enough? Must the screen depict kinetic action as in the study of Castiello et al. or will a simpler level be enough? In other words, what level of computer-generated simulation is required for the adaptive systems to respond as desired?

### Computer technology and neglect therapy

Within the research area concerning hemispatial neglect, experimental testing varies from simple interaction with keyboard, button and mouse that seldom creates an illusion of immersion, to fully immersed virtual reality systems (Rose, Brooks, & Rizzo, 2005; Tsirlin et al., 2009). However, most of this research is mainly directed towards improving the sensitivity of testing procedures (Anton, Hershler, Lloyd, & Murray, 1988; Baheux, Yoshizawa, Seki, & Handa, 2006; Broeren, Samuelsson, Stibrant-Sunnerhagen, Blomstrand, & Rydmark, 2007; Chiba et al., 2006; List et al., 2008) and has only just begun to consider the field of improving training methods (Ansuini et al., 2006; Katz et al., 2005; Kim et al., 2007; Turton et al., 2010; Webster et al., 2001).

Our study emphasises the importance of test and measures when implementing computer-based therapy, which works in the real world. Our study was on the absolute low end scale of immersion but we still managed to create a reasonable result after testing various conditions. This holds promise for the future. Although it is generally agreed that virtual reality technology has a huge potential within research on training and therapy of cognitive functions, virtual reality therapy will require much more research and development before becoming generally available for clinical work. Regardless of whether therapy is based on a simple PC and a touchscreen or on elaborate virtual reality technology, careful testing and measurements are needed to ensure that the therapy and tests do in fact target the systems we want to train. In the process, this research may reveal new knowledge about functions and dysfunctions of the brain.

## CONCLUSIONS

This study was initiated to test the effects of implementing Prism Adaptation Therapy on a computer. We chose the after-effect as a measure of efficacy and

compared the after-effect of two computer conditions with that from the standard physical box. The study revealed that in visuomotor tasks, it is important to provide feedback on the action in a manner which targets the systems that are involved in the adaptive processes. Knowing the task, understanding the task and even executing the task correctly are not always enough to produce the desired effects.

Translating therapy from paper-and-pencil to computer requires a thorough analysis of the individual elements making up the therapy. The translating process may assist in revealing unknown aspects of the working elements of training but it emphasises the need for careful testing of the resulting conditions.

Last but not least, this study confirms the need for further research in the field of computer-assisted neurorehabilitation which in turn may provide further insights both into normal cognitive function and cognitive deficits following brain injury.

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## USING ARTIFICIAL INTELLIGENCE TO CONTROL AND ADAPT LEVEL OF DIFFICULTY IN COMPUTER-BASED COGNITIVE THERAPY – AN EXPLORATIVE STUDY

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Within the field of cognitive rehabilitation after brain injury, rehabilitation training is constantly adjusted to match the skills and progress of the individual patients. As no two patients are alike in functional injury and recovery, it is a challenge to provide the right amount of training at the right level of difficulty at any given time.

This study investigates whether a modified version of the artificial intelligence (AI) reinforcement method called the “actor-critic method” is able to detect response time patterns and subsequently control the level of difficulty in a computer-based, cognitive training program. The efficacy of the AI logic was tested under the actual training conditions of a brain-injured patient.

The results showed that the AI controlled training system was able to learn and adjust fast enough to control and adapt the level of difficulty of the training to match the changes in the patient’s abilities over a three-week period.

**Keywords:** Reinforcement Learning, Cognitive Rehabilitation, Adaptive Therapy, Actor-critic, Adaptive Progression

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### INTRODUCTION

Over the past decade an increasing amount of evidence supports the notion that cognitive functions injured from trauma may recover, at least partially, through training and therapy that target different aspects of brain plasticity (Kleim & Jones, 2008; Friedemann Pulvermüller & Berthier, 2008). As with healthy brains, certain elements such as the intensity of the training, the type of feedback provided and the progression of the level of difficulty seem to be important, general aspects of the more recent type of therapy used experimentally in the rehabilitation of cognitive deficits (Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Friedemann Pulvermüller & Berthier, 2008).

In methods like cognitive Constraint Induced Aphasia Therapy, one of the key elements is the personalized in-

tensive training which challenges the patient gradually with progressively harder tasks (Friedemann; Pulvermüller, et al., 2001). However, to advance the training at the right pace and to the right level of difficulty is perhaps one of the hardest challenges for the therapists to do correctly, as performance of patients may fluctuate from day to day. First of all, no two brain-injured patients are alike even when diagnosed with similar afflictions. This means that training-progress may vary substantially from patient to patient. Even slight differences in impairment may impact the way training will affect progress and amelioration making it extremely difficult to determine how fast to advance with the training (e.g., Wilson, Gracey, Evans, & Bateman, 2009). Secondly, even with the same category of affliction, what is considered to be hard or difficult may vary from patient to patient (Wilson, 1998). Thus, the combination

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of parameters that determine the level of difficulty may very well differ substantially from patient to patient.

It therefore seems advantageous to study systems that may monitor the activity of the patient and be able to adjust parameters intelligently to match individual progress and deficits. However, this poses considerable challenges to the training system itself. First, it has to be able to monitor and detect consistent progress during training under realistic training conditions where progress may not be linear or constant and where measurements may be influenced by factors not under immediate control, such as the current condition of the patient. Secondly, the system has to be able to assess the ability of the patient quickly and consistently in order to select a correct set of parameters controlling difficulty level at any given time during training. In essence, the system must be able to adjust its behavior according to the individual effect of parameters, some of which may be known, some of which may not be.

Some computer-based cognitive training systems do offer automated progression in level of difficulty, most of them through a “staircase” progression whereby the program increases the general level of difficulty from one level to the next when the patient masters a certain percentage of the tasks at one level (Sturm, Willmes, Orgass, & Hartje, 1997; Wertz & Katz, 2004). In other cases the training progress is administered by the therapist, who is then required to monitor the progress and offer increasingly harder challenges (Pedersen, Vinter, & Olsen, 2001).

To some extent, challenges and requirements to intensive computer-based therapy for cognitive rehabilitation match those of computer game-play. Artificial intelligence (AI) has been used successfully in games to solve similar challenges of adjusting computer-controlled adversaries to match the skills of the game player at any given time (Bourg & Seemann, 2004; Spronck, Sprinkhuizen-Kuyper, & Postma, 2004). The research in this field has proven that certain machines learning AI algorithms are fast and efficient enough to learn and subsequently adjust game-play in real time to the constantly evolving skills of the player (Ponsen, Spronck, Munoz-Avila, & Aha, 2007; Spronck, et al., 2004).

#### PURPOSE

The purpose of this study was to explore whether an AI engine, based on the actor-critic machine-learning logic,

would be able to control the multidimensional progression of level of difficulty (LOD) as defined by three different parameters in a computer-based, cognitive training program for patients with acquired reading difficulty after brain injury known as pure alexia. In particular, the question was whether the engine would be fast and adaptive enough to compensate for fluctuations in the performance of the patients over time and be able to detect the subtle differences in the effect on difficulty provided by each parameter. This article specifically deals with the technical aspects and results of the study. The rehabilitation aspects and results from this study will be presented elsewhere.

#### CONSIDERATIONS REGARDING THE ARTIFICIAL INTELLIGENCE AGENT

##### LEARNING AGENT

The term “learning agent” refers to AI agents or programs that are able to learn about the environment in which they operate. This knowledge is in turn used to improve the agent’s ability to make appropriate choices of action. Learning can be achieved in several ways through different types of feedback. Usually, the way AI learning is achieved is categorized in three groups: supervised learning, unsupervised learning and reinforcement learning (Russell & Norvig, 2003). The difference being that in supervised learning the agent is initially taught correct behavior from samples of input and corresponding output. The outcome of this supervised teaching is a performance function which may then act as an expert system capable of solving problems of a similar kind. In unsupervised learning, the agent is searching for patterns in input and establishing rules based on those. Decision trees are examples of results of unsupervised learning (Russell & Norvig, 2003).

Reinforcement learning (RL) originates from psychology research, where reinforcement learning is thought to be one of the fundamental ways living beings learn from interacting with the environment. Similar to living beings, computer programs can learn through trial and error (Sutton & Barto, 1998). The RL agent learns about the appropriateness of selected actions through rewards and punishments after execution of behavior without prior knowledge of the environment (Russell & Norvig, 2003; Sutton & Barto, 1998).

##### THE CHOICE OF AI METHOD

In this study, the principal requirement for the AI algorithm was that it was learning quickly, was flexible and did not unduly impact the computer as the training program needed to respond rapidly and appropriately to the

actions of the test subject. The so-called actor-critic method from the RL category was chosen as it had previously been proven able to learn and optimize selection of actions quickly and easily in the research field of computer games with similar challenges (Spronck, Ponsen, Sprinkhuizen-Kuyper, & Postma, 2006; Spronck, et al., 2004; Spronck & van den Herik, 2005).

In research the term “Game AI” often refers to the appearance of intelligent behavior of computer-controlled game characters (Spronck & van den Herik, 2005). A large portion of game AI is often either fixed state machines or scripted logic due to the complexity in using and adapting the computational logic into usable, programmable entities (Bourg & Seemann, 2004; Galway, Charles, & Black, 2008). Recent research, however, has tried to establish usable solutions to game AI based on reinforcement learning techniques (Spronck, et al., 2006; Spronck & van den Herik, 2005).

Spronck et al. (2004) had successfully implemented and evaluated a solution based on a combination of dynamic scripting and a slightly modified version of the temporal difference (TD) learning methods named actor-critic methods. Using these methods they had optimized the selection of available actions for computer-controlled non-player characters (NPCs) in a role-playing game to set a level of difficulty that would challenge the player’s skills appropriately. By matching NPC strength to the strength of the player at a given time the player would stay motivated for gaming.

Since Spronck’s team (2005, 2006) had already tested the actor-critic logic against other RL techniques such as the Monte Carlo methods and Q-learning, and found it most suitable with regards to speed and impact, it seemed prudent in this study to build upon their actor-critic findings given the fundamental similarities in the requirements to the AI logic.

#### THE ACTOR-CRITIC METHOD

The actor-critic methods differ from other TD-learning methods in that the policy is independently represented by a structure known as the “Actor.” The estimated value function is known as the “Critic.” The Critic must learn and adjust the value of actions selected by the Actor through the sensory information from the environment. Since learning takes place in real time, the critic must learn and criticize any current action followed by the actor; this is also known as on-policy learning (Sutton & Barto, 1998).

#### THE AI ENGINE IN THIS STUDY

##### THE MAIN LOGIC

The actor-critic method used in this study consisted of three parts: (i) an actor that selected the appropriate parameter settings from three databases, (ii) a fitness function that converted the results from the actions to a numeric representation which were then passed to the third part, and (iii) the critic, that adjusted weight values for each action chosen thus raising or lowering the probability of the action to be reselected. Figure 1 shows the architecture of the agent.

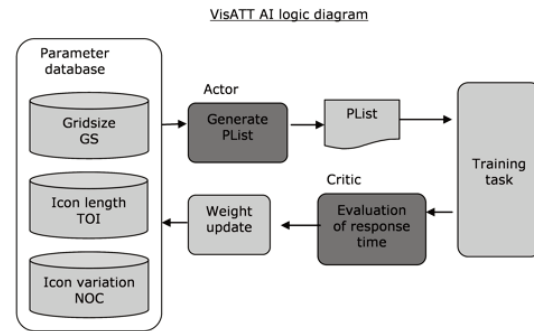


Figure 1. The architecture of the AI engine used in the VisATT training program.

The AI engine had no pre-established knowledge of the environment. The engine learned the appropriateness of a given set of parameters during actual training by examining sensory input in the form of response times achieved at any given time and continuously adjusted the choice of parameter settings.

Before each trial, the actor of the AI engine selected one setting from each of the three parameter databases based on the following algorithm:

##### Algorithm 1: Action selection (ACTOR)

```

1: Clear Plist();
2: k = 0;
3: for each parameterDB do
4:   sumWeights = 0;
5:   for i=0 to parameterDBSize-1 do
6:     sumWeights = sumWeights+parmDB[i].weight;
7:   end for
8:   fraction = Math.random()*sumWeights;

```

```

9:   sum = 0; j = 0;
10:  selected = false;
11:  while (not selected) do
12:    sum = sum+parameterDB[j].weights;
13:    if (sum>fraction) then
14:      selected = true;
15:      Plist[k] = parameterDB[j];
16:      k = k+1;
17:    else
18:      j = j+1;
19:    end if
20:  end while
21: end for

```

The probability that a specific setting for a parameter was chosen was influenced by the weight value attached to each setting. The sum of all weights defined the selection space. The size of each weight made each setting more or less visible within this selection space. Using a randomly generated selection criterion, it was possible to ensure a certain amount of exploration, since even large weights did not guarantee 100% selection each time. Initially, all weights were set to the same value of 100.

The critic of the AI engine receives the response time from the trial and determines the fate of the selected parameter settings:

#### Algorithm 2: Action evaluation (CRITIC)

```

1: medianRT = dampenInput(responseTime);
2: fitvar = AIFitness(medianRT);
3:
4: for i = 0 to Plist.length-1 do
5:   Plist[i].ParameterDB.weight = Plist[i].ParameterDB.weight * fitvar;
6:
7:   // Ensure exploitation across the range
8:   if Plist[i].ParameterDB.weight < atMin then
9:     Plist[i].ParameterDB.weight = atMin;
10:  end if
11:  if Plist[i].ParameterDB.weight > atMax then
12:    Plist[i].ParameterDB.weight = atMax;
13:  end if
14:  i = i+1;
15: end for

```

#### THE AI ENGINE FITNESS FUNCTION

The criterion for success for the AI engine was determined by measuring the time from the target icon was presented in the middle of the panel until the time the correct button was pressed (the response time). Two criteria set the lower and upper limit for an acceptable response time (see Figure 2). If the subject's time fell within these criteria, the LOD was acceptable. If response time fell beneath the low threshold (tooEasy), LOD was deemed too easy and the weights for the parameters selected would be reduced making those parameters less eligible for selection. Similarly, if the response time fell above the upper threshold (tooHard), LOD was deemed too hard and the weight of the parameters involved was reduced.

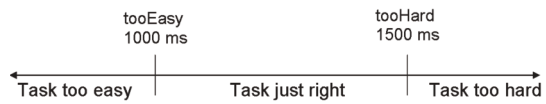


Figure 2. The tooEasy/tooHard range which determines fitness of chosen actions.

A bottom limit value of 20 as the lowest and 600 as the highest weight setting ensured that all parameters would remain eligible for selection allowing the difficulty to be reduced if necessary. This logic would ensure that as response times to a certain parameter setting would improve, the parameter would eventually drop below the tooEasy/tooHard threshold causing a new setting to be favored and selected.

#### Algorithm 3: The fitness function (AIFitness)

```

1: if responseTime < tooEasy then // Check if this was too easy
2:   return 0.9;
3: else
4:   if responseTime > tooHard then // Check if it was too hard
5:     return 0.95;
6:   else
7:     return 1.05; // Just right
8:   end if
9: end if

```

The setting of the Easy/Hard range in this study was calculated by testing a range of settings and measuring

which settings had an effect. A rule of thumb from all the completed tests seemed to suggest that 35% of all response times during a random 200-task session must be within the Easy/Hard settings. Using this rule of thumb, the subject's ideal setting proved to be 1000/1800 ms as opposed to normal controls, which estimated the setting to be 1000/1500.

#### METHOD

The AI engine was developed in Java and incorporated into a computer-based cognitive training program for visual attention (VisATT). As described above, the purpose of the engine was to monitor subject performance during training and constantly try to adapt the LOD of the training to challenge the subject's abilities. The adaptation in this case was done by adjusting the weights of three parameters according to a fitness criterion. The weights assigned to each parameter made the parameters more or less likely to be selected, resulting in an individualized increase or decrease of LOD as defined by the combination of the three parameters.

The testing of the engine was done as part of a real training program to place a maximum stress on the AI engine. It would have to perform rapidly and flawlessly under "noisy" conditions, where patient performance would potentially be influenced by a number of known, as well as unknown, factors. Quantitative data was recorded for each trial.

#### TEST SUBJECT

The subject was a right-handed male who, in 2005 at the age of 47, suffered a cerebral hemorrhage following thrombolysis treatment of a pulmonary embolism. As a result, the subject was left with an upper right quadrantanopia and subsequently diagnosed with pure alexia (letter-by-letter reading). Reaction times in single word reading were measured by a voice-key test administered by a trained neuropsychologist three months post injury. This showed a word length effect of 380 msec per letter ( $r^2 = .130$ ,  $F(1, 50) = 7.5$ ,  $p < .01$ ) for words of three to nine characters and a mean response time of 1,973 msec. In winter 2005/2006 the subject attended a rehabilitation program at the Center for Rehabilitation of Brain Injury (CRBI), of which the last two months were dedicated to daily intensive training aimed at improving reading abilities. Neuropsychological tests conducted in March 2006 at CRBI showed that the subject's performance was within the normal range compared to Danish norms, except for three scores on tests that involved psychomo-

tor speed and alphanumerical material. In April 2007, two months before this study, the subject was retested on the reading test mentioned above. The results showed a word length effect of 270 msec per letter ( $r^2 = .351$ ,  $F(1, 70) = 37.8$ ,  $p < .001$ ) and a mean response time of 1,717 msec. Further comprehensive investigation and assessment of this patient's injury, reading skills and neuropsychological profile may be found in (Starrfelt, Habekost, & Gerlach, 2010).

#### TRAINING SCHEDULE

The total amount of training consisted of one uninterrupted 30-minute session per day, seven days a week, for three weeks, totalling approximately 13,500 trial tasks – a trial constituting the task of pressing a button with a target icon as fast as possible. After each training session, data on the current status of the parameters was saved in order to allow training to recommence at that level the following day. Prior to the initiation of the training period, the test subject trained for three days to become acquainted with the functions of the system. The data from these tests was excluded from the measurements presented here.

All training took place at the subject's home once a day. The subject was free to choose the time of day to maintain motivation and to avoid interference with other unrelated activities planned during the three weeks of training.

#### EQUIPMENT

The subject trained on a laptop PC running Windows XP and Java 1.5. The primary input device was a 17-inch LG 1730SF TFT finger touch monitor placed horizontally on a table with the touch-screen facing upwards to reduce fatigue during training. Screen resolution was 1280x1024 pixels.

#### SOFTWARE

The training software consisted of two components: the AI engine and the training program for visual attention (VisATT), which was controlled by the AI engine. Both components were designed and programmed by the author especially for this study to ensure proper and timely interaction between the components and the logging of relevant data that could be used later on in simulations of activity.

#### DATA COLLECTION

The primary internal data collection was done automati-

cally by the training system which recorded trial event data during training sessions directly onto a disk to prevent loss in case of unscheduled interruptions. The secondary internal logging happened at the end of the session, when the “x” at the top right corner of the training screen was pressed. This signaled the end-of-session and the current AI settings (weights and values) and the last-played date would be saved for subsequent resumption.

#### THE TRAINING PROGRAM - VISATT

The training program was developed specifically to train letter span and object detection speed. The design and implementation of the training were done in collaboration with the neuropsychologist who had previously worked with the test subject.

For each trial, the subject was presented with a target icon in the middle of the screen surrounded by a set of selection buttons (see Figure 3). One and only one of the surrounding selection buttons would match the target icon in the middle. The rest of the buttons, the distractors, would have icons of a similar type and length. For each trial, the subject had to search the surrounding buttons for the button matching the target icon, and then press the one matching button as quickly as possible. The number of buttons, the length of the word on the icon and the variety of distractor words were determined by the values of three parameters. The buttons would be distributed evenly on the screen in predetermined patterns, ensuring an approximately equal distance from the center.

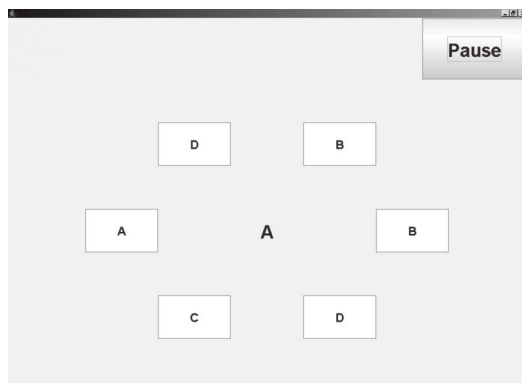


Figure 3. The basic training panel layout. The target icon in the middle of the screen is “A” and the button choices are “D,” “B,” “B,” “D,” “C,” “A.” The person training must find and press the “A” button to the left as quickly as possible.

The test subject was told to press the “PAUSE” button if he needed a break for some reason during training. This would cause the response time data from this trial to be discarded in the internal calculations. A special log record was created to identify this situation.

#### THE VISATT PARAMETERS

The LOD is often closely linked to the task being trained. To define what makes a task more or less difficult is in some cases obvious, for example, when juggling balls in the air, adding a ball will increase difficulty. However, in rehabilitation it may not always be equally obvious what will be difficult for a patient and what will not. It most likely depends on the type and location of the injury, previous abilities, motivation and future goals of the patient (Wilson, 1998). For this reason, the training program was designed specifically for a patient with pure alexia. Pure alexia is most often characterized by a decrease in reading speed corresponding to the word length as well as degraded processing of visual objects (Leff, 2004; Starrfelt, Habekost, & Leff, 2009). The following parameters were chosen to be the most appropriate to represent elements that would be expected to increase or decrease LOD by, in various ways, increasing or decreasing visual the complexity of the visual stimuli presented:

1. Grid size – the number of buttons shown on the screen. Only one button will contain an icon matching the center icon, and the other buttons act as distractors. The LOD is increased as the number of buttons increases by adding visual elements to be searched through and ignored. There are eight settings (2, 4, 6, 8, 10, 12, 14, 16) for this parameter corresponding to the number of buttons displayed.
2. The icon length (TOI) – the word length. There are four settings (1, 2, 3, 4 letters) for this parameter indicating the length of the icon word.
3. The icon variation factor (NOC) – the variety pool size. As only one button, the target button, may contain the center icon, the rest of the buttons, the distractors, are displayed with similar types of icons selected from a pool. The NOC parameter determines the variety pool size. The setting range of this parameter is 2-28 with two-step increases.

#### RESULTS

During testing, the logs revealed that the AI logic did not initially work as intended. The correlations between raw



response time and parameters were not significant enough for the AI engine to detect changes in the performance of the test subject, due to the fluctuations in response time. This is a fairly common problem in psychophysical experimental psychology when using raw response time data to analyze correlations in tasks which require a high degree of concentration and quick responses (Howitt & Cramer, 2005). Dampening the influence of noise in the data was therefore done using a small, rolling, temporal median table of response times for each parameter setting. Thus, the median value calculation required a set of raw response times for each setting of the parameters, but not the combinations of settings. A fair amount of trial and error showed that the median response time calculated on the basis of a small rolling history of the five most recent response times for each setting was sufficient to dampen noise and at the same time maintain the responsiveness to changes in the subject's ability. This result was passed to the AI engine instead of the raw response time.

#### THE AI CONTROLLED LEVEL OF DIFFICULTY

The selection results were compiled from the daily event log files. Training tasks with wrong buttons activated were removed from the results as were the records made due to pressing the PAUSE button. The reason for this was that these records were considered exceptions and typically the cause of extreme outliers. Analysis showed that erroneous button presses constituted less than 1% of the total number of button presses and they were there-

fore determined by the author to be insignificant indications of performance in this case study.

Figure 4 shows the changes over time in the preferred setting of the GS parameter controlling number of buttons. Initially, a setting of 2 is weighted highest and selected most often, but already after six days of training two buttons (GS=2) begins to be too easy and four buttons (GS=4) becomes the preferred setting. Towards the end of the training period six buttons (GS=6) begin to be chosen more and more often. The subject did not reach a plateau during the three weeks of training.

The same pattern was seen for the second parameter, the word length parameter (TOI). Figure 5 shows that towards the end of the training period the settings 1 and 2 were favored above 3 and 4.

The last parameter, the NOC parameter, showed no correlation between median response time and setting causing the AI engine to select settings totally at random (see Figure 6).

#### DISCUSSION

##### THE USE OF AI FOR ADAPTIVE CONTROL IN A COGNITIVE TRAINING SYSTEM

The research question in this project was whether or not the chosen AI algorithm was suitable for controlling and adapting LOD in a cognitive training program under real-life conditions. A reinforcement learning al-

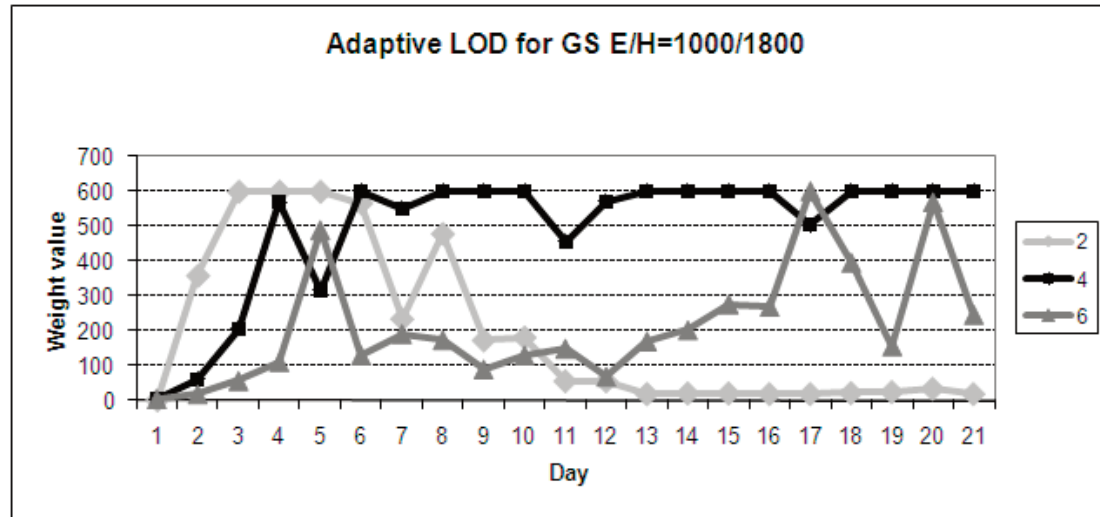


Figure 4. The weight assignment of the eight settings of the GS parameter (no. of buttons) during the three weeks of training.

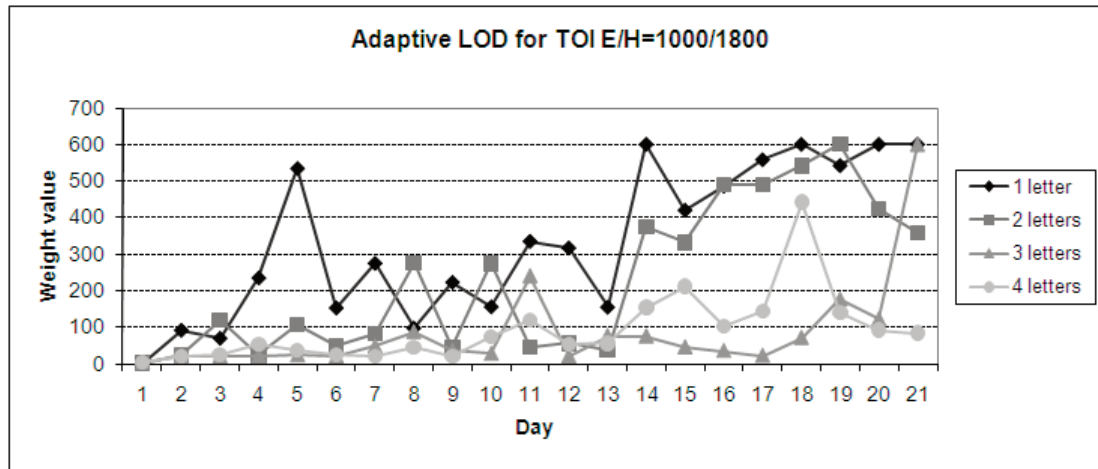


Figure 5. The weight assignment of the four settings of the TOI parameter over the three weeks of training.

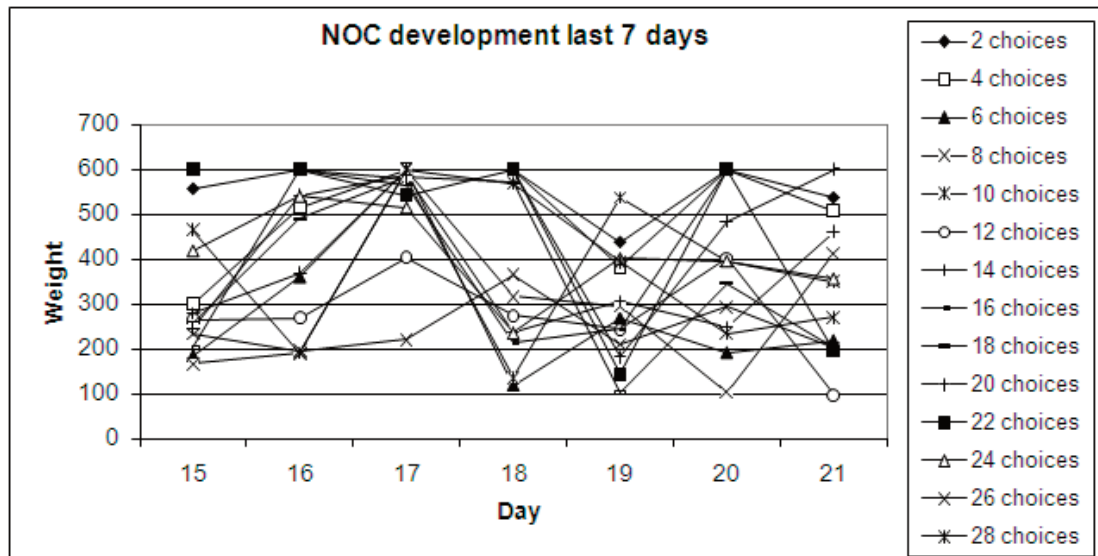


Figure 6. The weight assignment of the 14 settings of the NOC parameter over the last week of training.

gorithm was chosen as the AI method for two reasons, its ability to learn in an unknown environment and its fast learning rate. As the weight distribution for the parameter settings in Figures 4 and 5 showed, the AI engine and logic managed to distinguish a group of settings as being an appropriate LOD as opposed to others that were either too hard or too easy. It also showed that the selected settings changed as values changed from day to day depending on the effects measured by the system through response times. Figure 6 shows the

results from the third parameter, the NOC, which controlled the variety of icons within the remaining distracters. This parameter never seemed to stabilize at any preferring setting.

When considering the conditions of the environment in which the AI engine managed to work, the use of AI technology in cognitive training looks promising. The AI engine itself was a simple implementation offering many opportunities for improvements of the algorithms



used to control weights and determine fitness. In this implementation the free assignment of weight values worked to isolate optimum settings, but there may very well be further possible improvements in using some of the culling and clipping techniques that Spronck et al. (2005) suggest in their research.

#### THE EASY/HARD SETTING – THE SUCCESS CRITERION

The success of the AI engine in this study depends on the measure of success used to rate the selected actions. If these measures are not distinct, the agent has no way of learning or change actions.

In this study the measure of success was determined by the predefined Easy/Hard range against which the response time was compared and selections subsequently rated. However, the Easy/Hard setting turned out to be difficult to estimate. If the Easy/Hard range was too wide, it was too insensitive to changes in performance related to individual parameter changes causing assignment of the same fitness value to too many adjacent settings of the parameters. This resulted in too much variation in the selection of parameter settings. If on the other hand, the Easy/Hard settings were too narrow, all settings were judged to be either too easy or too hard causing a leveling out of the influence of the weights which resulted in random selection rather than selection by appropriateness. As no established model for determining the settings existed, a set of guidelines was developed, which was based on observed results from testing the programs on volunteering fellow students and friends.

The heuristic nature of the guidelines, however, does not ensure optimal settings, so this is definitely an area that requires further investigation and automation.

Another subject for future research will be to investigate whether the AI engine in fact needs an independent measure of success for each parameter controlled. The TOI parameter did not seem to converge around one or two settings as the GS parameter did. One explanation could be that the optimum Easy/Hard range for one parameter differed from the optimum Easy/Hard range of another. Another explanation could be that three out of four settings did in fact provide equal levels of difficulty. It will require further tests and analysis to determine whether this is in fact the case.

From another perspective, the Easy/Hard range could

be viewed as the primary parameter of LOD which needs to be estimated, at least initially, in order to match a certain level of ability. With further research it might be possible to automate the estimation and initial settings of the Easy/Hard range using the same AI engine, but by turning the logic around so the Easy/Hard range becomes the parameter to be estimated from a fixed task set of one or more parameters in the parameter database. Another possibility would be to let the therapist set the range, but that would require some kind of assistive tool for the therapist to be able to judge what would be suitable.

#### PARAMETER SELECTION

The decision to let the AI engine control three parameters was in part based on the fact that in Spronck's research (2004, 2005, 2006) the AI solution was able to handle this, and in part based on the fact that this would reflect the conditions of challenging cognitive training. However, the relationship between success criteria and parameters in Spronck's game were, in retrospect, much simpler than those met in this study. In the case of Spronck, his success was determined by a Boolean variable (win or lose), whereas mine was determined by the Easy/Hard range of response times which was directly influenced by the parameters and indirectly by other factors outside my control. Also, the potential difference in impact of the several parameters in combination was not an issue in Spronck's solution.

Although the use of three parameters did make the study more demanding and raised new questions, it did show that the AI engine was able to detect correlations between response time and two of the parameters. In an actual training environment there may be other parameters exerting influence on the response time during a session. Secondary factors such as fatigue, motivation, concentration and the visuo-motor movements involved in pressing buttons, may directly or indirectly influence the performance of the test subject. In theory however, the influence from these factors presumably affect the parameters in equal measures like background noise.

This study faced some of the same difficulties facing therapists when trying to translate the difficulties introduced by impairment into trainable parameters controlling level of difficulty. As opposed to the modified fitness function of Spronck's design (Spronck, et al., 2006; Spronck, et al., 2004; Spronck & van den Herik, 2005),

the algorithms in this study had no way of ascertaining the effect is of the individual parameters. This is definitely an area for further investigation and improvement of the AI engine.

Trying to define a programmable logic for the engine has made me even more convinced that technology can play an important role in assisting therapists in planning, designing and executing training.

#### LIMITATIONS IN THE STUDY

Due to the investigative nature of this study, there were several areas that would require more appropriate control in future studies. In particular, the noise created by the physical arm movements of the subject. To create a realistic training environment, the buttons on the screen were not laid out at the same physical distance from the center of the target icon. The reason for this was that the subject was allowed free movement of the arm and was not required to reposition the arm after each pointing trial, so it was deemed less essential in the initial study. In future studies, this is an area which could be improved upon. However, the fact that the AI algorithm managed to adjust, despite this, does suggest that the algorithm is fairly resilient to noise.

#### CONCLUSION

The results from this project demonstrate some of the conditions to be met if training is to be controlled by the AI actor-critic reinforcement logic (Sutton & Barto, 1998). In terms of controlling level of difficulty it means that:

- The response time must be influenced by task difficulty. The harder the task, the longer the response time. This must be verified with patient data.
- Task difficulty must be expressible through a number of parameters.
- The criterion for a challenging level of difficulty must be defined as a response time range with an upper and lower level within which the patient must operate in order to progress.

- Each parameter must indicate a range of settings from low to high LOD.

When considering the conditions of the environment in which the AI engine managed to work, the use of AI technology in cognitive training looks promising.

This study was explorative and intended to develop and test AI controlled training to determine whether this type of advanced computer technology could, in fact, be used under the conditions of cognitive training. The conclusions from this study were:

- That it was possible to develop an AI engine able to measure and adjust LOD using reinforcement learning methods.
- That it was possible for the AI engine to work under the very difficult conditions of the real-life cognitive training of a patient suffering from alexia. By introducing the temporal median filter to dampen the noise in the raw input, the AI engine did manage to control all three parameters and show clear indications of being able to adjust LOD as the patient's skills improved. The weights controlling the AI parameter selection converged to an optimum for the two parameters controlling number of buttons and length of word that had a clear correlation between measured median response time and LOD setting. The third parameter controlling variety of words on the distractor buttons that had no correlation showed an even distribution of weights across settings.

The next research step will be to test the AI engine under different training conditions and with different training programs. The hope is that this type of intelligent training tool will assist in the wider study of the effects of intensive, adaptive cognitive training of patients with cognitive impairments after brain injury.

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**DISSIMILAR OUTCOMES OF APPARENTLY SIMILAR  
PROCEDURES AS A CHALLENGE TO CLINICAL  
NEUROREHABILITATION AND BASIC RESEARCH – WHEN  
THE SAME IS NOT THE SAME**

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## **ABSTRACT**

In the study of the brain and how it adapts to changes or injury, researchers sometimes come across situations where apparently similar types of tests or training do not achieve similar outcome results. This is true, in particular, within the field of computer-based rehabilitation where paper-and-pencil tests and training is converted to computer. This paper raises the attention to the fact that supposedly similar settings may not, in fact, elicit similar results and caution therapists and researchers who work with rehabilitation of brain injury. The paper suggests that the underlying mechanisms behind this may be illuminated by using the REF (Reorganization of Elementary Functions) model and suggests that further research into the use of advanced technologies such as computer-generated virtual reality is required.

**KEYWORDS:** computer-based rehabilitation, cognitive rehabilitation, REF-model, after-effect, adaptive processes, brain injury, plasticity.

## **Introduction**

Cognitive rehabilitation training of brain injured patients is often a highly demanding endeavour – not only with respect to the efforts required by the patient, but also with respect to the time-demands on the therapist. New developments suggest that at least partial functional recovery may be achieved through intensive training which challenges the impaired function through increasingly more difficult tasks [e.g., Kleim & Jones, 2008; Pulvermüller & Marcelo, 2008]. However, increased training will make even further demands on the scarce time of the therapist. A potential solution to these increasing demands may be increased utilization of computers in the testing and especially training of patients during posttraumatic recovery. An added benefit of such a technological development will not only be precise and continuous collection of data but also carry the potential for “online” adjustments of training (e.g. regarding the progression of level of difficulty) and the delivery of consistent and timely feedback during training. Additionally, computers may provide a safe – but real-life-like – training environment through the use of virtual reality. Since the advance of the personal computers and minicomputers in the 1980’s there has been a certain level of experimental introduction of computers in rehabilitation training and a certain level of success has been achieved [Ansuini et al., 2006; Katz et al., 2005; Kim et al., 2007; Smith et al., 2007; Webster et al., 2001]. Today, computers are being used extensively within diverse areas of cognitive rehabilitation such as the modelling of damaged functions; assessment of cognitive dysfunction; training and therapy; cognitive prosthetics and within assistive technologies.

However, the expanded use of computerized methods challenge our knowledge of how to “translate” the traditional “paper-and-pencil” versions into computerized methods particularly within the field of assessment and training of brain injured patients. At first glance, such an endeavour may appear relatively unproblematic, but the process of translation requires a thorough understanding and consideration of the underlying cognitive processes, which are involved and activated during the execution of the traditional version of the test or training. If not, the subsequent construction of a computer-based solution may inadvertently add or remove features, which may be relevant or even vital for the therapy to be effective. Using computer-based solutions may change the way the patient interacts during testing or training – for instance with regards to visuomotor and visuospatial activity and feedback. This, in turn, may influence the effect of the training and subsequent adaptation. The steps of the translational process may indeed prove significantly more challenging as it basically rests on the assumption that a therapist or researcher is fully aware of all the underlying cognitive processes involved in the outcome of a particular test or training procedure. This emphasizes the need not only to conduct a thorough testing of the computer-based solution itself but also to analyse whether the solution has the wanted impact on the cognitive system.

In the following, we will provide examples, which illustrates that “the same is not always the same” in terms of cognition and behaviour in what is assumed to be similar environments. Through the use of the REF (Reorganization of Elementary Functions) model [Mogensen, 2011a, 2011c; Mogensen & Malá, 2009], we will try to explain why apparently similar behaviours may not be associated with activation of the same cognitive elements and neural processes in rehabilitation.

## **Dissimilar performance on apparently similar tests – human studies in neglect**

Our understanding of the correlation between the tools used in assessment and the cognitive skills being assessed is repeatedly being challenged by results from studies both on human subjects and within the use of animal models.

In the rehabilitation of brain injured patients suffering hemispatial neglect, Prism Adaptation Therapy (PAT) has been shown to be rather successful in ameliorating some of the effects of neglect [Frassinetti et al., 2002; Rossetti et al., 1998]. In traditional PAT, the patient trains by executing pointing movements with their hand from sternum to one of three spatially separated targets. The upper extremities are hidden beneath a screen to prevent the patients from seeing the actual movement. A PAT session consists of three steps: 1) A pre-exposure step in which the patient is directed to point to either of the three target in a random fashion. The patient receives no feedback on precision. 2) An exposure step in which the visual field of the patient is diverted 10 degrees to the right through the use of prism goggles. The patient receives feedback on pointing precision by being allowed to see the fingertip when pointing at the targets. Most patients will gradually adapt to the perceptual shift in the visual field during this step. 3) A post-exposure step where the patient again removes the prism goggles and point to targets. The effect of the prism adaptation is measured by observing the size of a relatively brief after-effect which manifests itself as leftward off-target pointing movement after removing the prism goggles. The after-effect is thought to be a measure how the visuomotor system has adapted to the brief change in the visual field [Fernandez-Ruiz & Diaz, 1999]. A crucial element of this therapeutic procedure is the feedback provided to the patient regarding the precision of the target pointing during the training period [e.g., Frassinetti et al., 2002; Sarri et al., 2008; Serino et al., 2006, 2007].

A recent attempt to convert the traditional version of PAT to a computer-based version [Wilms & Malá, 2010] clearly demonstrated that apparently similar executions did not result in similar effects. In a number of experiments, both healthy subjects and patients suffering hemispatial neglect were subjected to a single session of both a traditional and a computer-based session of PAT. The rather surprising outcome of the direct comparison between results from the two sessions was that the size of the after-effect depended on whether or not the subjects received direct feedback regarding the pointing precision by actually seeing their fingertip. Other types of feedback via icons on the computer screen failed to produce an after-effect of similar amplitude (ibid).

In an earlier study Luh [1995] wanted to determine if a leftward bias observed in line bisection tasks for healthy test subjects was related to perceptual asymmetries or a bias in the motor component. In one experiment 24 persons were given the same line bisection test in two versions, i.e. one pencil-and-paper and one implemented on computer. The experiment demonstrated that the observed bias from the manual line bisection task disappeared when the line bisection task was performed on computer. Luh ascribed this difference in task outcome to the difference in motor involvement (arm movement) in the two versions.

However, both examples illustrate that a seemingly insignificant difference may have a big influence on the test subject and may lead to inconclusive results or even wrong assumptions about the efficacy of computer-based therapy. The benefits of computerizing testing and maybe especially rehabilitative training procedures are challenged in case such problems occur in the “translation” of the traditional version into a computerized method. But – as will be discussed below – an even broader perspective grows from such discrepancies.

### **Dissimilar performance on apparently similar tests – animal models**

The phenomenon of different outcomes of what was believed to be identical procedures in training and testing of neural and cognitive functions is, however, not restricted to the domain of computerization of human procedures. Research within animal models of the cognitive



consequences of brain injury provides additional examples of situations in which “the same is not the same”.

Lepore et al. [1985] tested in cats whether information relevant to the performance of a visual discrimination task could be transferred subcallosally between the hemispheres. Cats subjected to split-brain operations (lesions of the corpus callosum) trained a visual discrimination task with visual information presented to only one hemisphere. Subsequently, the performance of the same task was tested with visual information presented only to the contralateral (previously untrained) hemisphere. A successful performance of the visual discrimination task under such circumstances would indicate a subcallosal transfer of information. When the visual discrimination training was performed in a classic two-choice discrimination box (a maze-type setup) in which food was offered as reinforcement, no transfer of information between the two hemispheres was found. However, when the animals were trained and tested in a “Lashley-type” jumping stand which punishes the wrong choice by letting the animal jump into a locked door, animals subjected to the split-brain procedure demonstrated an interhemispheric transfer of information. Although a number of aspects differentiate the two procedures, a priori one would have expected the two to yield the same result.

An impaired performance of spatial delayed alternation tasks is often considered the diagnostic tool when determining whether or not a group of experimental animals (be it rats, monkeys or other species) have suffered a lesion or functional disturbance within the prefrontal cortex or associated structures such as the prefrontal part of the neostriatum [e.g., Mogensen, 2003; Mogensen et al., 2007, 2008]. In spatial delayed alternation tasks, two spatially separate target positions (e.g., arms within a maze or cups towards which a monkey can reach) are offered to the animal. Initially, the animal may freely select one or the other of these positions and will receive a reinforcement. After this initial choice and a short delay, the animal is required to choose the previously non-chosen position in order to receive a reinforcement. If the same position is selected, no reinforcement will be given and a time-out period is imposed. On each subsequent trial, the animal is required to make alternate selections of position (each time after a short delay). Repetitive visits to the same position are never reinforced. Mogensen et al. [1987] tested if two variants of spatial delayed alternation would reflect impairments of the prefrontal system. Rats subjected to lesions of the prefrontal part of the neostriatum (in addition to undercutting of the prefrontal cortex) were tested in spatial delayed alternation in both a T-maze and an operant chamber. In the T-maze, the animal chooses between the two spatially separate arms of the T-shaped maze – and the animal is removed from the apparatus between trials. In the operant chamber, the animal chooses between two spatially separate retractable levers situated in a wall of the chamber. The animal remains in the chamber between trials – but the levers are retracted. While the general requirements of a spatial delayed alternation task were implemented in both experimental setups, only the T-maze based version was able to significantly reflect the injury to the prefrontal system (although the same animals were tested in both setups) [Mogensen et al., 1987].

As should be clear from these examples (further examples may be found in Mogensen [2003; 2011b]) even in animal models two implementations of the same task may reflect a particular type of brain injury in vastly different manners. However, when subjected to a traditional analysis of the cognitive demands, the two versions of the test may appear to be similar.

The types of results described above constitute a significant challenge within several fields related to brain injury and neurorehabilitation. At the conceptual level, a major challenge is that although presumably similar procedures of tests and training methods have been developed in order to fulfil

all currently known cognitive demands – and which falls within the existing cognitive classification systems – the dissimilar outcomes testify against the validity of the prevailing understanding. Clearly, basic research into brain injury and posttraumatic recovery is presented with a conceptual and experimental challenge.

For this reason, a direct translation of established test and training procedures to computerized methods in neurorehabilitation is likely to create more obstacles than may originally be expected. In essence, it would require a full understanding of the cognitive mechanisms of traditional tests – as well as the general process of posttraumatic functional recovery – to achieve a successful translation of traditional tests into computerized procedures. Obviously, the development of individual test procedures may not have to depend on a more complete conceptual understanding. For instance, further research into the elements important with respect to the sight of the pointing finger in the procedures addressed by Wilms and Malá [2010] may be able to pave the way for the development of a more successful computerization of the PAT-procedure. Furthermore research aimed at identifying – in humans as well as in animal models – the crucial aspects differentiating the cognitive and neural demands of two test manifestations may provide data of importance in understanding not only the individual tests, but the intricate functional reorganizations of the injured brain. Consideration must therefore be given to whether the aforementioned conceptual developments within neurorehabilitation are relevant to the presently discussed issues.

Some suggestions as to why two apparently similar procedures do not result in the same effect may be found in a recently proposed neural and cognitive model [Mogensen, 2011a, 2011c; Mogensen & Malá, 2009]. While primarily developed to account for the apparent contradiction between regional functional specialization within the brain and the ability of the injured brain to “functionally recover”, this model also carries important implications regarding clinical neurorehabilitation and for the possibility of translating one manifestation of a test or training procedure into another potentially computerized manifestation. It should be stressed that although developed in the context of brain injury and posttraumatic rehabilitation, the REF-model describes processes which are believed to be occurring in the intact brain as well as posttraumatically [Mogensen, 2011a, 2011c].

### **The REF-model**

The concept of functional localization – the idea that various brain structures are uniquely specialized in a particular type of information processing – is supported by a wealth of data. The two major sources of such support are, (a) lesion studies in which brain injured patients or experimental animals exhibit predictable patterns of behavioural, cognitive and/or emotional changes after a particular type of brain injury and (b) neuroimaging studies in which particular brain regions are rather consistently activated in cases of similar types of stimulation or activity. Such local specialization of brain regions [e.g., Coltheart, 2001; Kringelbach & Rolls, 2004; Monakow, 1914; Selnes, 2001] does, however, appear to be contradicted by the fact that even in the mechanically lesioned brain – where the lost brain structure is clearly not re-established – a more or less complete level of posttraumatic functional recovery may occur [e.g., Buller & Hardcastle, 2000; Mogensen et al., 2004, 2007; Panksepp & Panksepp, 2000; Ramachandran & Blakeslee, 1998]. One of the goals of the REF-model [Mogensen, 2011a, 2011c; Mogensen & Malá, 2009] is to explain how posttraumatic functional recovery is possible in spite of a strict functional localization. In the REF-model, a distinction is made between two levels of “function”. On the one hand, the term Elementary Function (EF) is introduced and defined as the information processing performed by an individual brain structure or substructure. Such EFs are the basic information

processing units of the brain and, according to the REF-model, all the EFs mediated by a brain region are permanently lost in case of irreversible injury to that region. On the other hand, the “functions” typically characterized in the language of neuropsychology and neurology (e.g., episodic memory, expressive language, egocentric spatial orientation) are in the REF-model considered to be “surface phenomena” of behaviour and/or consciousness. It is at the level of the surface phenomenon that the functional recovery is observed – since a “function” is considered to be “recovered” when the individual behaviourally manifests a performance indistinguishable from the pretraumatic situation. The bridge between the EFs and the surface phenomenon is a kind of cognitive/neural “program” named an Algorithmic Strategy (AS). An AS consists of a unique combination of EFs and the interconnections between these. At the neural level, an AS is mediated by the neural substrates of all its constituent EFs plus the projections and synaptic connections mediating the information flow between these basic processing modules. At the cognitive level an AS can be seen as a “program” in which the information processing is achieved by a unique combination of (/information flow between) the basic information processing by EFs. It is the activity of an AS that gives rise to a particular surface phenomenon – be it a behavioural performance or a conscious manifestation. It is, however, also stressed by the REF-model that a particular surface phenomenon may apparently be achieved by a multitude of ASs. That is: although, in a strict sense, various ASs will manifest themselves in dissimilar surface phenomena, the distinction between such surface phenomena may be impossible to realize by the individual having the experience and/or an observer scoring the task performance of for instance a patient or an experimental animal, unless a highly sophisticated analysis is performed [Mogensen, 2011a, 2011c; Mogensen & Malá, 2009].

When the brain is injured, all EFs mediated by the brain region affected by the damage are irreversibly lost. And, consequently, all ASs within which these EFs are represented are lost as well. Surface phenomena achieved via the activity of the lost ASs will become unavailable and what is traditionally seen as the symptoms of that type of brain injury is the absence of those surface phenomena, which are now unachievable. Subsequently, the posttraumatic functional recovery is achieved by the creation and/or activation of alternative ASs. If these alternative strategies are able to achieve surface phenomena, which are completely or at least to an extent indistinguishable from those originally lost, the observed situation is a complete or partial functional recovery. These alternative ASs must obviously consist of combinations of EFs mediated by the spared parts of the brain. Neurally, they represent the neural substrate of such remaining EFs and the neural connections allowing a relevant information flow between these localized circuits.

The posttraumatic process leading to a functional recovery always includes some type of reorganization. The process may include plastic reorganizations at two separate levels. In all cases there will be a cognitive and neural reorganization associating a particular situation/problem/domain with the activation of a particular – alternative – AS. At the neural level this cognitive association between a situation and the activation of an AS include synaptic reorganizations within the parts of the brain mediating the processes of selection and evaluation of cognitive/behavioural strategies. If one of the pretraumatically existing ASs is able to achieve a satisfactory level of competence by its activation, this may be the only level of reorganization necessary for that recovery process. If, however, no available AS turns out to be adequate, the second level or reorganization is also called for. At this level – the “reorganization of elementary functions”, which has given the REF-model its name – the EFs of the remaining parts of the brain are reorganized and connected into novel ASs. This is achieved via mechanisms more or less comparable to the backpropagation algorithm [e.g., Rumelhart & McClelland, 1986; Werbos,

1994]. Only when a novel AS has been created and selected will the recovery process be manifested at the surface level. In these cases of recovery processes, patterns of synaptic connections are modified even in the connections between the neural substrates of individual EFs.

As mentioned above and by Mogensen [2011a, 2011c], the processes described by the REF-model are believed to occur in intact as well as injured brains. The mechanisms mediating posttraumatic functional recovery are likely to have evolved as part of the neural and cognitive mechanisms allowing flexibility and problem solving in the intact individual. Whenever somebody encounters a situation demanding problem solving (in the broadest sense of the term) for which there has not already been established a procedure/strategy leading to successful task solution, the described mechanisms of search for an adequate AS and potentially even creation of a novel AS are initiated. What is special about the posttraumatic situation is that even situations, for which solution mechanisms were available pretraumatically, may now have the appearance of being “novel” [Mogensen, 2011a, 2011c].

According to the REF-model [Mogensen, 2011a, 2011c; Mogensen & Malá, 2009] both of the above mentioned levels of reorganization and plasticity are achieved in a constant interaction with the environment. It is the environmental feedback during attempted task solution (in the broader sense of the word) that provides the basis for the reorganizational and plastic processes. Consequently, the plastic reorganization may be relatively specific to a specific environment.

The surface phenomenon – which in the present context means the performance on a particular variant of a test or training procedure – reflects the selected AS. Viewed in this manner it may be easier to understand why even apparently insignificant modifications of the procedures can have drastic consequences with respect to the ability of a test to reflect the consequences of brain injury and for that matter, the accomplishment of a positive therapeutic outcome through rehabilitative training.

In the ongoing research aimed towards an improved understanding and characterization of the EFs, studies addressing closely related test variants, which become differentially affected by a particular type of brain injury, are a promising avenue. By being at the formal level so similar and still differentially affected by brain injury, these procedures may reveal important information regarding the ASs and their constituent elements. This in turn will provide information about how the brain learns and adapts to changes in the environment and how training needs to be provided in order to achieve a positive outcome.

The REF-model also carries a clear warning regarding the extent to which one should expect the results of rehabilitative training to generalize across tasks. As emphasized above, by Mogensen [2011a, 2011c] and by Mogensen and Malá [2009], novel ASs are constructed via backpropagation mechanisms, which are the result of situational feedback regarding the success or failure of an attempted task performance. Additionally, already existing ASs are selected for utilization in a particular context via the feedback provided in that context. Given the specific nature of ASs, this may bring into question to what an extent the task solution achieved in one situation can be applied by the same individual in a different setting. This may be especially true in case of an injured brain where the total repertoire of EFs and ASs is more limited than what would otherwise be the case.

The latter point emphasizes the final and potentially most problematic way in which neurorehabilitation has to face situations in which “the same is not the same”. Although

rehabilitative cognitive training may be able to achieve a significant level of apparent functional recovery under institutional or other relatively controlled settings, it may remain in question to what an extent such a positive outcome is able to generalize to the real-life situations of the patient. Specific training procedures – be it in a computerized environment or not – may become more and more efficient. But unless it is constantly tested to what an extent these therapeutic results actually generalize to the subsequent real-life situations of the patient, many of the results of neuropsychological training of the brain injured individual may be of little or no benefits in other contexts of the patient's life. Therefore, it is important to emphasize two ways in which therapeutic procedures can be improved.

Firstly, it needs to be consistently validated whether or not a rehabilitative training method generalizes beyond the actual training situation. This validation process is in many ways a parallel to what is being conducted within other fields of computerized training aimed at utilization in a more real-life situation. One such issue is the question whether training performed in computer-based flight simulators generalize to actual flight – which might be the case in some but clearly not all instances [e.g., Gopher et al., 1994; Hart & Battiste, 1992]. If, in the brain injured patients, generalization does not occur, it may be an indication that the perceived correlation between observed surface phenomena, injury and therapy is not valid. Furthermore, in addition to the current neurological and neuropsychological tests, it is essential to include assessments that can be performed in a setting, which closely resembles real-life in order to determine the extent of damage and subsequent improvement.

Secondly, in cases where the complexity of correlation between injury and observed surface phenomena is poorly understood, the general rehabilitation program for each and every patient should include attempts to assure the highest possible degree of “ecological validity” of the training procedures. The rehabilitation programs will have to include elements, which bridge the institutional training and setting to the subsequent life at home and at the workplace. Only by exposure to the complexity of the real-life tasks in training can the brain be induced to form and select ASs of value to the patient's particular circumstances of life.

We speculate that the tendency towards computerization may – when properly applied – turn out to be one of the elements in this bridge between institutionalised training and the subsequent life of the patient. The use of portable computers and PDAs (potentially including the utilization of GPS-based localization and navigation) may allow many types of rehabilitative training to continue beyond the borders of institutions and into the real-life situation of the patient. Within the institution itself, aspects of the real world life of the patient can be simulated and addressed even without leaving the institution through the use of computer-simulations and virtual reality settings.

When building virtual realities, however, it has to be emphasized that even taking into consideration all levels of present day knowledge regarding the essential components of a particular situation, may be insufficient in achieving the desired rehabilitative goal. As the study of computerized feedback in Prism Adaptation Training shows, something as simple as whether you see your own finger or a representational “x” as feedback on a pointing task may in fact dramatically affect the adaptation effect on the brain [Wilms & Malá, 2010]. Even in this promising development of a merger between technology and neuropsychological rehabilitative training, clinicians and researchers alike are challenged to look beyond the surface phenomena and remain open to the ways in which normal and injured brains reorganize while interacting with the environment.

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