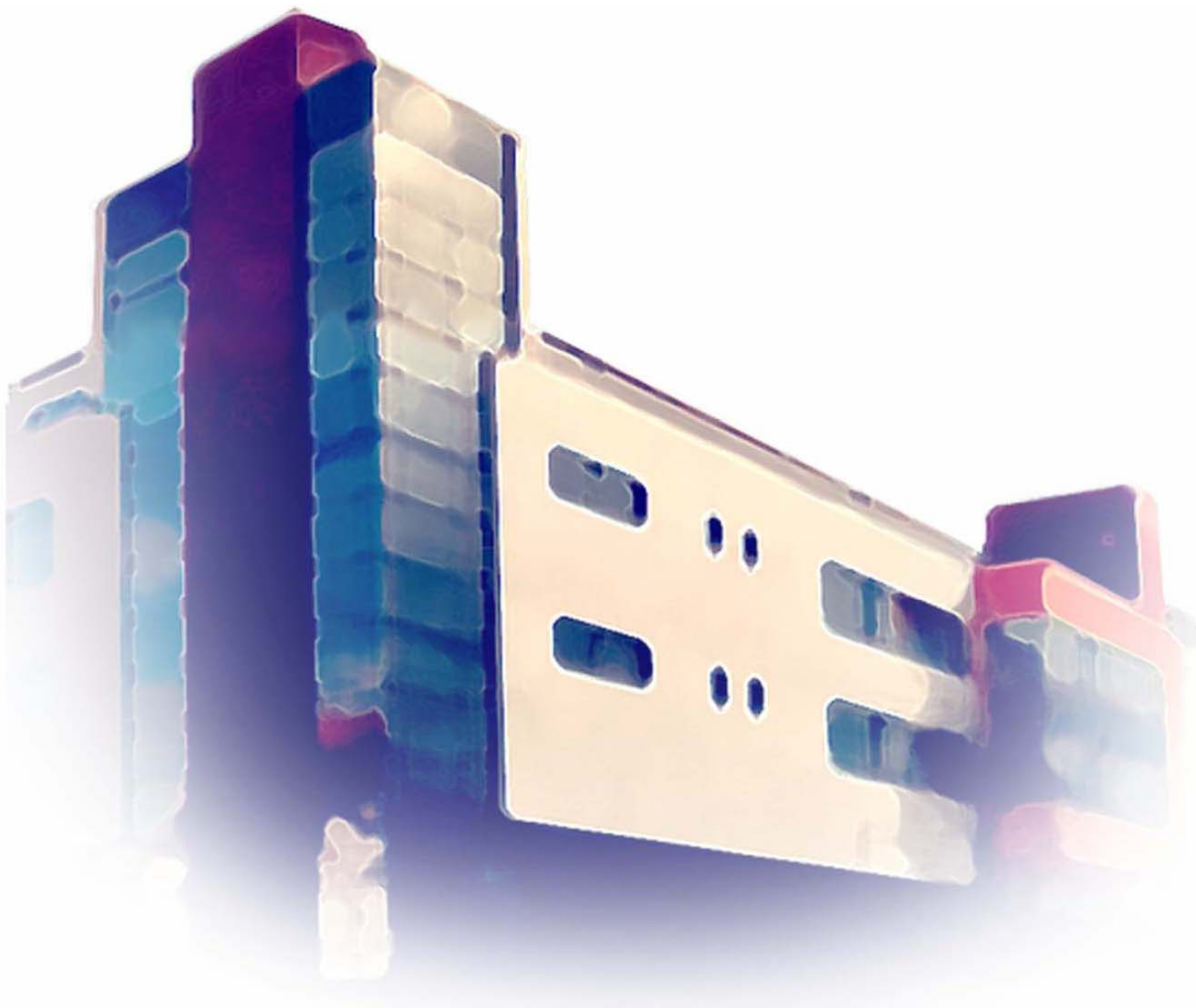


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MINI: Mechanisms In Neuropsychological Issues



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MINI

Mechanisms In Neuropsychological Issues

Masters Study Project
Institute of Cognitive Science
University of Osnabrück, Germany

Final Documentation
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Forward

The Master's Study Project component of the Master Programme in the study courses of cognitive science was conceptualized to fulfil the goal of developing the scientific and professional competence of students who are pursuing advanced knowledge in cognitive science. It is in principle the place where we can actually put the idea of interdisciplinary study into action. And a ground where we can put into practice all the theoretical constructs we learn in our courses. Appropriately then, we had a group of 10 talented and motivated people with diverse backgrounds and skills. As all of us have discovered across the course of our cognitive science experience, this is both a blessing and a curse.

MINI as a specific instantiation of this idea of interdisciplinary skill building was born like many things however, of pragmatic constraints. That is, opportunity and desire. The opportunity came in the form of a chance meeting at a university cultural function of Herr Prof. Dr. med. Friedrich Albert, a neurosurgeon, and Herr Prof. Dr. Ing. Claus Rollinger, at that time the director of the "Institut für Kognitionswissenschaft". Being both a highly skilled neurosurgeon and the directive physician in the neurosurgery at the Paracelsus Klinik, Prof. Albert naturally knows a lot about the brain. However, his experience with the brain was in terms of repairing its accidents, and his curiosity and scientific drive led him to be interested in its functional properties—that is, cognition. Of course, this being what we study at the IKW, a conversation with Prof. Rollinger naturally led to the idea of a collaboration between Prof. Albert and someone from the IKW.

This is where desire entered the evolution of MINI. I am one who has spent many hours for example tediously measuring hippocampal and amygdale volumes on MRI slices, and am fascinated by the functional properties of cognition that arise from this squishy lump of cytoarchitectures sitting inside everyone's skull that we alternately call the "mind" and the "brain". Many students of the study courses cognitive science share this fascination. Although I currently work in issues of cognition at a more abstract level than the wetware, I was happy to have a chance to supervise some students who were interested in using cognitive tasks to investigate theoretical questions about the brain/cognition relationship, with the gracious help of individuals who had brain surgery. It also seemed a way to integrate the IKW with our surrounding community of the "real world".

There is a saying: “Life is what happens when you are making other plans”, and this somewhat summarizes our ensuing project. That is, as with any collaboration starting without an infrastructure, it seems we made plans and built more infrastructure than made progress towards solving any issues in cognition. However, this process was exactly the kind of experience that does not come out of books and lectures and exams. The entire project time was a great revelation for me: the course of seeing how determined everyone was to learn things such as data analysis, experimental design, and remaining positive in the face of all the normal frustration of seemingly endless implementational and bureaucratic obstacles. Not to mention at times, our own inertia. Thus in the end, it is a pleasure to see how everyone evolved during the project, and a pleasure to see so much development work accomplished in the affective priming paradigm, the Morris Water Task, and perspectives in Neuroethics.

Following now is what we wanted to do, what we did, what we learned, and where we want to go next. Enjoy.

Jacqueline Griego
Osnabrück, 2004

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Part I

Overview

Introduction

This documentation describes the MINI study project taking place within the Cognitive Science Master Program at the University of Osnabrück. For 18 months, the group of up to twelve people has been involved in developing and executing a scientific project around the possibility to examine neurological patients.

“The way is the goal”, an old proverb says. This is certainly true for student projects – many of the things we did, we did for the first time. Learning about experimental, organisational and also social dimensions of scientific team work constitutes, in our view, a big part of what the idea of a study project is all about. But beyond that, we have worked hard to create results possessing relevance in themselves. When faced with major complications, we adapted our initial plans in order to put into use the existent theoretical and experimental know-how built up by then. We hope to present conceptual and empirical work that has value outside the scope of the study project as well.

The goal of this document, hence, is two-fold. On the one hand, we want to provide an insight into the many aspects of the work that constituted our project. On the other hand, we want to present the outcome of this work in a way that is easily accessible for prospective readers outside the project - they should be able to take up the results of what we did without the need to digest our internal affairs. Therefore, we compiled our results into three “stand-alone” papers – one for each of the three big sub-parts of our project: Affective Priming, the virtual Morris Water Maze and Neuroethics. These papers are available as part of this documentation, separately via our project homepage, and will be - or have already been - submitted to journals.

This short introductory section will continue with some history and organizational information. The main section of the documentation will deal with the three main areas mentioned above. Each of these areas entails two texts: The first describing the internals concerning that part of the project, the second describing the results of our research in a paper-like format. In the concluding section, we will come back to a project-specific perspective in order to summarize and evaluate the project as a whole.

History of the MINI project

The MINI project is a cooperation between the Paracelsus Klinik Osnabrück and the University of Osnabrück. This cooperation was established by Prof. Dr. Albert, Leitender Arzt at the Neurosurgery of the Paracelsus Klinik and Dr. Jaqueline Griego, Master Advisor in the Cognitive Science Programme.

Dr. Jaqueline Griego's aim was to establish a connection to the "real" life, where students can make experience with patients in the clinic, and possibly have the opportunity to see brain surgery. There students can see a brain in reality - rather than on schematic drawings in the well known books. Moreover, students can experience how patients with brain lesions are treated in hospital and are able to study the deficits resulting from the lesion.

Prof. Dr. Albert's interest was to do a new study and to gain a new insight into actual research in cognitive neuroscience. He mostly has to do with patients before and shortly after surgery and is interested in the more long-term, functional implications of the lesion and the ways and degrees people can recover from that.

The first phase: Finding a question

In the initial phase from February 2003 to August 2003 members of the MINI project were Prof. Dr. Albert, Dr. Jaqueline Griego, Ute Kreitz und Jiayong Liu.

The name MINI stands for "Mechanisms In Neuropsychological Issue". Ute and Jiayong, under Jackie's supervision, did literature research in order to find an interesting hypothesis for the project. During this process Jiayong build the first MINI-webpage to store information, papers and links.

They dealt with saliency maps, attention and priming until they came to the phenomenon of visual neglect. Visual neglect is a disorder of spatial attention caused by damage to posterior parietal cortex (e.g. stroke, infarct, tumour). The most persistent symptom appears after right inferior parietal lesion. People are no longer able report or orient to stimuli on the contralateral side to the lesion. So they decided to make a proposal for an experiment examining the visual neglect and related disorders like blind sight and extinction.

The second phase: Designing the experiments

In October 2003 the second phase of the MINI-Project started. New Master students joined the project, now MINI was no longer a mini project in the sense of few participants. The new members were Stanley James, Cristiane Kabisch, Oleksander Kolomiyets, Jens Kunkemöller, Christian Mühl, Saskia Nagel, Nicolas Neubauer and Frank Schumann. At this point we had Ute's and Jiayong's proposal, which provided us with a research question. But we still had to find a proper methodology.

Again we searched the literature for papers which dealt with the neglect phenomenon and with hemispheric differences. We found a paper by Rémy Versace¹ which dealt with affective priming and a paper by Hans-Otto Karnath which used lateral presentation to figure out the role of the superior temporal cortex. We decided to do an experiment, which combined those two experiments. This meant that we do an affective priming experiment with lateral presentation of the primes and central presentation of the target pictures.

A new question

Another research question that emerged was spatial navigation. During our literature research we found that patients with lesions in the hippocampus have difficulties to remember spatial cues and so have a poor performance in spatial navigation. Since Prof. Dr. Albert told us that, in his department, patients with hippocampus-lesions are relatively frequent, we decided to expand our research on spatial navigation and hippocampus-lesions. Subjects with lesions in the hippocampus should be tested with the virtual Morris Water Maze, a simulated swimming pool in which the subjects have to find a platform hidden underwater. By using the Morris Water Maze we wanted to replicate the experiment by R.S. Astur. The virtual Morris Water Maze is a new program with which it is possible to conduct this experiment with humans which originally was done with rats. In the original experiment rats were put into a swimming pool filled with non-transparent liquid, where they had to find a hidden platform. The virtual Morris Water Maze simulates this experiment on a computer. It is like a 3D-Action-Game in which the subject has to navigate through a virtual swimming pool. The task again is to find the hidden platform.

¹ See parts II and III for references.

The definition of the methodology we would be using nearly marked the end of the second phase of our project. The last task we had to accomplish was the presentation in the Institute of Cognitive Science where we reported the research question, methodology, experiences with organisation, cooperation and tool use at that time. We gave our presentation end of April 2004, and from this point on we were ready to run our experiments as soon as possible. The only missing thing was the information from Prof. Dr. Albert when and where we could test which patient.

The Last Phase: Conducting the experiments

In April 2004, Ute and Jiayong officially left the project as, by then, they had been participating for one year. Still, they and the rest of us were looking forward to begin the experiments. However, this turned out to be complicated.

After we had designed our experiments properly we had made an appointment with Prof. Dr. Albert to demonstrate our experiments and to get his permission to run the experiments in the Paracelsus Klinik. It turned out we would need the permission of the Ärztekammer Hannover, too. We then had some problems with the administration of the Ärztekammer, which cost us 2 -3 months in which we could not run our experiments, until the ethics committee of the university declared our experiments as harmless.

Adapting

When it became clear that due to this problems, we would not be able to execute our experiments within the time frame of the project, we had to find a way to continue our project. The only chance we saw was to recruit our fellow students as participants. So we had to slightly change our research questions.

For the affective priming experiment there were not so many changes. We now were testing for the hemispheric differences in priming. We wanted to find out if it makes a difference whether a prime is presented to either the right or the left visual field.

For the Morris Water Maze experiment, we had more difficulties to find a new research question. Finally, we decided to look for sex-differences. So we had different setups for the Morris Water Maze program and were looking if women and men performed differently in finding the hidden platform.

Execution & Analysis

At the end of July we ran our experiments for about 3 weeks, with fellow students recruited via email. Each of us ran several experiments. Jackie advised us with the statistical analysis of the data.

August and September we spent analyzing our results, planning and writing this documentation.

We are now preparing for some of us to finally run the patient study we had originally planned in the near future.

Project and Experiment Organization

Meetings

During the project we organized regular weekly meetings for about 3,5- 4 hours at the office of Dr. Jaqueline Griego. A member of the project documented each meeting so we had the possibility to restore discussions and the most important points in working groups for solving current problems. Applied part and practical questions were discussed with Dr. Prof. Albert, when we visited brain-surgeries at the Paracelsus Clinic or at an meeting set up for that purpose at the University of Osnabrück.

As already mentioned, the MINI project gathers students with different interests and it became a ground to divide into working groups. So we had one group particularly concerned with the affective priming experiment (Frank Schumann, Stan James, Jens Kunkemöller), one for the virtual Morris water task (Christian Mühl, Christiane Kabisch, Oleksandr Kolomiyets), a group for ethics questions (Saskia Nagel and Nicolas Neubauer), a software developer group (Stan James and Oleksandr Kolomiyets), a web page group (Stan James and Nicolas Neubauer) and a problem coordinator (Christiane Kabisch).

Communication

As a project management tool we used the StudIp. StudIp was developed for supporting study processes between students and universities. StudIp provides useful functions for our project: Data archive, forums, course management, Wiki-webs, news and appointment arrangements and others. In spite of the fact that the StudIp is a powerful interactive tool, we had problems to understand its functionality, but in fact a lot of functions are new and helpful. As a common communicational tool between us we used e-mails.

The face of the project became a MINI Homepage:

<http://www.cogsci.uni-osnabrueck.de/~mini>

It is not just our official representing but also an interaction tool for all who is working and interesting for the project. The homepage is based on the very popular “blog-approach”. A blog is a journal that is available on the web. This approach helps to reduce the development time of the site and edit already existing pages by logging in. The project’s homepage consists of

following pages: About, Members, Problems, Progress, Resources, Experiment. All interesting information about experiments, project progress and experiments can be found on the web.

Experimental issues

The software development and testing parts of the project were done by project members. The development time was divided into small implementations solutions: Pilot experiment (release: January 2004) and AP experiment (release March - April 2004). We created an install version of the experiment and so we tried the program under different hardware and software condition that gave us some ideas to fix and better the software depending parts. Accordingly to Affective Priming paradigm we had precisely to follow experiment conditions, in particular visual angles, distances, sizes etc. We adjusted the program for a 17" flat monitor. Another aspects, which have not been discussed above, were provided by technical equipment. We installed a bitebar to fix a head and hold on the same visual line to the concentrating point, and a chair with variable height adjustment.

After a long waiting time for patients (conditioned ethics questions) participant enticement problem we solved by conducting promotional actions among students (announces, student's forums, etc.). Some of them already knew what the project is about, some students were interested in psychology or similar areas thus they also became participants of the experiments. At first moment it seemed to be complicated to get enough number of participants, but later it was not problem anymore except the female part of them.

Part II

Lateralized Affective Priming

Theoretical Background of Hemineglect and Affective priming

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Introduction and Relation to the Overall Project Goal

An overall goal of the project was to establish a cooperation with a local clinic to investigate cognitive functions such patients. Given this, a first part of the project involved to develop a scientifically promising research hypotheses for studies with patients. Another part of the project involved to derive an experimental paradigm to suitably examine these hypotheses.

This section documents our initial research interest, which, broadly speaking, fell into the area of visual attention and its disorders. After a review of the literature, we posed a hypothesis on residual visual processing abilities for affective stimuli in patients with hemineglect syndrom. We developed an affective priming paradigm with lateralized presentation of the priming stimuli as an indirect test to demonstrate that hemineglect patients can process affective visual stimuli at a very early and automatic level of processing in the neglected field.

This section also documents our second research interest that we developed in response to the prolonged delay we were faced with in getting the permission of the ethics comitte to carry out experiments with patients (see the section on the ethics review in part IV.1). Since the affective priming experiment developed for the neglect population uses lateralized presentation of priming stimuli, the same paradigm can also be used to investigate hemispheric assymetries in affective priming within a student population.

Then, in this section theoretical and methodological background of all these issues will be described in turn. Experimental results are reported in a stand-alone paper to be submitted (part II.2).

Initial broad Area of Research Interest: Visual Attention

We are exposed to an abundance of visual stimuli every day: lights flashing, cars zooming by, people crossing our way, fleeting facial expressions etc. In the human visual system, information is transferred between the retina and the brain at 10^8 - 10^9 bits per second. This exceeds by far “what the brain is capable of fully processing and assimilating into conscious experience” (Deco et al., 2002). So how do we select the information to which we react and how do we choose a particular behavioral program for responding to this information?

“The concept of attention implies that we can focus on certain components of the sensorial input, [...], by shifting the focus of processing activities in a serial fashion from one

location to another. This mechanism is commonly known as *selective or focal attention*” (Deco et al., 2002).

In other words, attention is a mechanism for dealing with the bottleneck of information processing. Without attention regulation we would orient towards everything that moves or appears around us, which would lead to a state of constant distraction. For example, as you read this sentence, your visual system must cope with two tasks: Each word needs to be identified and simultaneously all other competing visual stimuli must be ignored (Groh et al., 1996).

Back in 1867, Helmholtz referred to focal attention with the metaphor of a spotlight: the spotlight of attention illuminates a certain area of the visual field “where stimuli are processed in more detail [...]” and “[...] information outside the spotlight is filtered out” (Deco et al., 2002). According to the Helmholtzian theory, information in the visual field is processed in a serial fashion. James (1890) extended this theory by proposing that, when attention is dispersed, information across the entire visual field can be processed in a parallel manner.

Neisser (1967) then combined these two approaches: Visual search involves two stages – preattentive and attentive search. “The first *preattentive* part comprises processes that are fast, parallel and involuntary, and the second *attentive* part comprises processes that are slow, serial and voluntary” (Deco et al., 2002). In 1988, Treisman introduced a refined version of his feature integration theory: In the preattentive stage, a parallel process is employed to scan the entire visual field and to extract primitive features without integrating them. In the second, attentive, stage, particular parts information are serially integrated (Deco et al., 2002). Visual attention is only one of many forms of selective attention. However, it is the most studied and thus best understood form of selection.

First Research Interest: Unilateral Visual Neglect and other Disorders of Visual Attention.

The phenomenon of unilateral visual neglect is particularly suitable for studying the relations between visual processing and awareness. Visual neglect, also known as hemineglect or spatial neglect, is a frequent neurological “disorder of spatial attention that generally follows posterior parietal damage” (Farah, 1994), which is typically characterized by the loss of awareness and failure to report or orient towards stimuli in the contralesional side of space. This disabling condition is often the result of focal brain damage after a stroke, traumatic brain injury, tumor

and surgical resection. Broadly speaking, it affects the coherent processing of visual stimuli and the production of appropriate behavioral responses, which leads to “distractibility, errors of action, and poor sustained performance” (Whyte, Moss Rehabilitation Research Institute).

The different forms of visual neglect affect many activities of daily life. Patients with visual neglect pathologically direct their gaze away from the affected hemifield, and thus are oblivious to people and objects in their contralesional hemifield. Furthermore, they tend to omit left parts of words when reading or miss food on the left side of their plate. They also fail to recognize limbs on their left side, which may cause them to only dress or shave their right side. However, symptoms of neglect do not reflect any loss of intellectual functioning.



Fig. 1 The way neglect patients perceive their plate

In pure spatial neglect, the integrity of early visual pathways is given and patients do not manifest any visual field deficits like hemianopic patients (Marshall et al., 2002). Hemianopia produces defects similar to those observed with hemineglect, but here the impairment is the consequence of damage to the optic pathways in the brain. Although both patient groups misperceive their environment in a similar way, hemianopic patients suffer from *visual* impairment whereas neglect patients struggle with an *attentional* disorder.

Patients diagnosed with milder cases of neglect often experience visual extinction, which is the inability to detect a contralesional stimulus in the presence of a competing ipsilateral stimulus. However, single stimuli presented to only one hemifield at a time can be easily detected. Extinction is even more pronounced when two stimuli are presented that have identical attributes than when they have differing attributes. “Although most reports of neglect show deficits limited to the contra-lesional field, extinction can also occur when two identical stimuli are presented within the ipsilesional hemifield” (Battelli et al., 2003).

In most cases, the visual neglect syndrome is transient and symptoms subside after a few weeks or months. According to a review by Pizzamiglio et al. (2001), the recovery of cognitive functions is due to a “functional reorganisation of the central nervous system”. Imaging studies have shown a change in cerebral blood flow induced by the same task performed before and after recuperation from spatial neglect. Researchers assume this to be associated with an increased activation of spared cortical structures in the right hemisphere (Pizzamiglio et al., 2001).

Anatomy of Visual Neglect

Since early reports on patients with neglect, it has been believed that only lesions in the right posterior parietal cortex and the TPO junction (junction area between the temporal, parietal and occipital lobes) produce symptoms of visual neglect. Although these regions have been widely confirmed, they recently have become disputed, as additional pathologies that results in symptoms of visual neglect have been identified (Karnath, 2001).

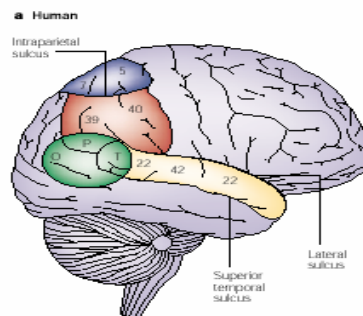


Fig. 2 The green area represents the TPO junction

Some studies suggest that lesions of the superior temporal cortex -- on the lateral surface of the right hemisphere -- are associated with visual neglect, particularly the superior temporal gyrus (STG) as well as the superior temporal sulcus (STS). Both structures are located between the ventral (‘What’) and the dorsal (‘Where’) stream of visual processing. The ventral stream projects from V1 to the inferior temporal cortex whereas the dorsal stream is connected to the posterior parietal cortex. The dorsal stream is believed to be critically involved in “spatial localization and the control of action” (Culham & Kanwisher, 2001). Damage to this particular

area leads to attentional deficits, spatial localization disorders and problems with sensorimotor coordination.

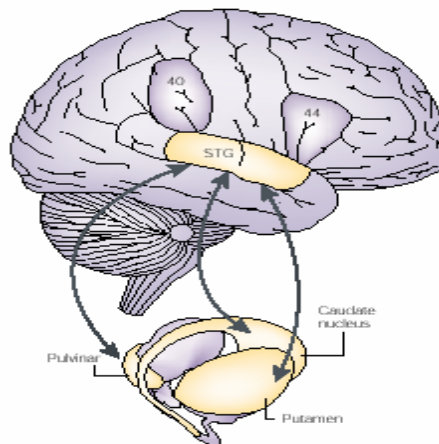


Fig. 4 Superior Temporal Gyrus (STG)

Mort et al. (2003) cite studies that have observed neglect with lesions of the right inferior frontal lobe, and subcortical structures, i.e. thalamus and basal ganglia. Furthermore, in their functional imaging study, Mort et al. (2003) mapped the location of certain lesions and found that “the most critical brain region associated with neglect [...] is the [angular gyrus] on the lateral surface of the inferior parietal lobe”. Additionally, the parahippocampal region on the medial surface of the brain is another area that needs to be damaged to produce neglect.

Despite this heavy debate about the exact location of lesions involved in the visual neglect syndrome, there is substantial consensus among scientists that these injuries occur predominantly in the right hemisphere. Only in very rare cases do we find patients with neglect that was caused by morbid changes in the left hemisphere.

In sum, visual neglect appears most often in right hemisphere damage, though there is not one clear critical area. Rather, it involves both various cortical areas (right parietal cortex and the TPO junction, superior temporal gyrus) and subcortical areas (thalamus, basal ganglia, angular gyrus). For a recent review on hemineglect see also Kerkhoff (2001).

Assesment of Visual Neglect with Line Bisection, Copying, and Cancellation Tasks

To assess the disorder of spatial neglect, many neurologists employ standard test batteries. “The symptoms of neglect are not 'all-or-nothing' and therefore accurate assessment of the severity of the condition is important” (Fairhurst et al., 1998). A traditional test of visual neglect is the line bisection task. Here, patients are presented with a horizontal line on a piece of paper and are asked to mark the middle of the line. They typically displace the bisection mark towards the side of the brain lesion (Ferber & Karnath, 2001). Other standard tests that are used to detect and quantify visual neglect include copying and cancellation tasks. These tests are generally brief and easy to administer at bedside.

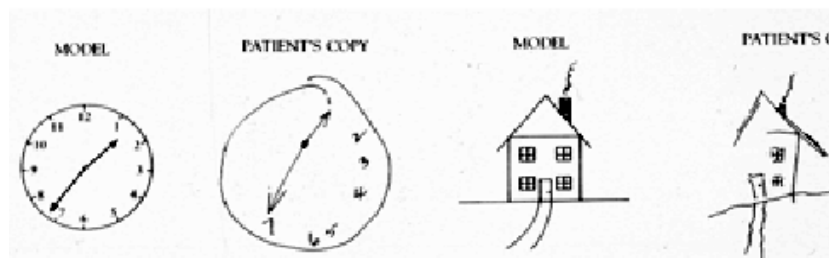


Fig. 5 Results of a copying test: only details from ipsilateral side

Studies have shown that different assessment tools have different degrees of sensitivity for detecting visual neglect. For example, the star cancellation task by Weintraub and Mesulam (1985) identifies patients with subtle and resolving neglect whereas the line bisection task may only identify those with profound neglect (Ferber & Karnath, 2001). Also, when compared with line crossing, the bells test (Gauthier, Dehaut, & Joanne, 1989) is a more sensitive measure of mild and moderate forms of neglect. Both, the bells and star cancellation test make use of distracter items requiring patients to perform a selection task rather than a mere detection task. Targets and distracter items are randomly arranged and the objective is to correctly identify the target items (Ferber & Karnath, 2001).

However, discrepancies in results on cancellation and line bisection tasks have raised doubts about the accuracy of these assessment tools. For example, Ferro and Kertesz (1984) observed a patient whose performance was impaired in both the cancellation and line bisection task two weeks after he had suffered a stroke. When he retok these tests three months after the onset of his disorder, he “performed normally on a cancellation task while showing significant rightward

deviations in line bisection” (Ferber & Karnath, 2001). The dissociation between performances may be due to the fact that each test requires the use of different cognitive processes.

In their study, Ferber and Karnath (2001) found that in a test battery the bells test and letter cancellation had the highest omission scores (61 and 62% respectively), indicating that these cancellation tests are most sensitive to detecting neglect.

Perimetrics measurements in the clinic are necessary to exclude visual extinction patients from the neglect population

Apart from general discussions about the accuracy of paper-based tests of visual neglect, for us particular limitation of these tests showed to be that they can not differentiate patients with a pure form of neglect from those with the similar, but milder syndrome of visual extinction, as needed for our experiment. As will be reported in the following, our hemineglect experiment aims to demonstrate residual processing in neglect in form of priming effects for lateralized presentation of primes into the dysfunctional (usually the right) hemisphere. To do so, we present a prime (only) a single prime either to the left or the right visual field in each trial. Yet, as reported above, visual extinction leads to impairment in visual processing only in the presence of two or more *competing stimuli*. Thus, patients with visual extinction will not experience symptoms of the neglect with only one stimulus. Rather, they process and perceive a single stimulus without substantial impairment. That is, they can be expected to have intact processing of single priming stimuli, as in our paradigm, and for this reason they also can be expected to show a priming effect. This effect, however, would be due to normally function visual processing of the primes, rather than due to residual processing in a neglect condition. Consequently, this means that in order to demonstrate residual processing in neglected parts of the visual field by means of lateralized priming effects, it is important to ensure a population of patients with pure neglect in which even the processing of single stimulus is severely impaired. Thus, we needed to exclude patients with visual extinction. Confounding both groups of patients would confound the results, rendering a reliable interpretation of found effects as residual processing in neglect impossible, as a possible effect found across all participants could be due to normal processing of a single prime in extinction rather than due to residual processing of a neglected prime.

Unfortunately, the common tests for visual neglect above present multiple rather than single stimuli, and thus can not differentiate between pure forms of the neglect and visual extinction. Therefore, tests such as line bisection can only be used to assess the degree of the impairment in

both pure neglect and visual extinction. But as both patient groups will score on them, these tests can not differentiate the two forms of neglect.

Fortunately, we can rely on the assessment of the visual field size by the ophthalmologist in the clinic to separate both patient populations. The standard procedure to determine visual field size involves systematic presentation of single light flashes across the entire visual field with a perimeter. As only one stimulus is presented at a time, this procedure is sensitive to the difference between pure visual neglect and extinction, and thus can separate both groups. However, perimetric measurements are too complex and time consuming to be repeated to control the state of the neglect directly prior to the experiment. Therefore, using a short and easy to administer test of neglect like line bisection as a control measurement, we can only confirm the actual severity of the neglect prior to the experiment, but we can not confirm the exclusion of extinction patients from our population. To our knowledge, no similarly quick and easy test that is sensitive for the difference between visual extinction and pure neglect exists.

Residual Visual Processing Abilities in Hemineglect

Recently, there is accumulative evidence (e.g. in Farah, 1994) that visual neglect does not affect the complete visual system. Rather, it is likely that patients still process some implicit residual visual information, even though they may not be able to use it in the service of behaviour or conscious perception. This appreciation of the neglect syndrome is quite recent. Previously, as Berti et al. (1992) point out, “[it] has often been assumed in neglect, the [contralesional] stimuli are not elaborated or are discarded very early in the visual processing”, and thus are not processed any further. However, a series of clinical and neuropsychological studies provides evidence for “intact implicit perception of ignored stimuli in neglect” (Schweinberger et al., 2001). For example, Berti et al. (1992) cite a case of a woman with severe visual neglect, who was asked to determine the difference between two drawings of a house: in one drawing the house was intact and in the other one it was on fire. When the features relevant for discrimination were presented to the contralesional side, the woman denied any difference between the drawings. However, when she was asked in which house she would “prefer to live” she would repeatedly choose the intact house, which lends support to the occurrence of “high order visual processing” without awareness (Berti et al., 1992). Furthermore, Schweinberger et al. (2001) refer to a case study in which the neglect patient demonstrated

associative priming by ignored words in the left hemifield, which indicates that neglected words can be processed up to the level of semantic activation. Additionally, Vuilleumier and Schwartz (2001) found that two neglect patients could detect pictorial drawings of an emotional image like a spider presented to the left visual field more often in a stimulus detection task than pictorial drawings of a neutral image like a flower. This suggests that emotional information about a stimuli in hemineglect is still being processed, that it might capture attention and in consequent cause enhanced processing of that stimuli and increased conscious perception of emotionally connotated stimuly.

Affective Priming as an Indirect Means to Test Residual Processing in Hemineglect

Our choice of testing residual processing in hemineglect is motivated by two reasons. First, Farah (1994) suggests that residual information in hemineglect, and the extend to which it is processed, is generally detectable only by means of indirect tests². Priming effects are promising candiditates as such an indirect measure; they show the processing of a prime indirectly by measuring how it interferes with a target task. Thus, the priming paradigm seems a promising means to detect residual information processing in neglect in form of priming effects in the neglected hemisphere.

Second, the general question we wish to contribute to is “as to what level of information processing stimuli in the neglected hemispace are ignored” (Schweinberger et al., 2001) or are being processed. On the one hand, we expect that in hemineglect early and automatic levels of information processing are preserved more than other, later levels of information processing. Therefore, we suppose that early and automatic processing levels should be most easily detectable. In the affective priming literature, such early and automatic processes have been frequently suggested as a realiable source of affective priming with brief stimulus onset asynchronies (SOA) of below 300 ms (see below). Hence, affective priming provides an indirect test to demonstrate residual processing in hemineglect. In addition, as is shown in the following, affective priming reliably seems not to involve other later processes such as semantic processing. It therefore selectively evokes information processing at an early and autonomic level of

² Though see Vuilleumier and Schwartz (2001) for a direct influence of residual processing of affect on conscious perception.

processing, isolating it from processes occurring later on. Thus, on the other hand, we also think that if affective priming can be shown in patients with hemineglect, they will selectively demonstrate early and automatic processing of affect.

The Affective Priming Paradigm

This section, if not otherwise noted, is based on a review on affective priming by Fazio 2001 (but see also the review of Klauer, 1998). Affective priming is a version of the classical priming paradigm, using affectively connotated stimuli as primes and/or targets. The phenomenon of priming shows an influence of the prime stimuli on the performance of a later target task, typically in form of shortened or prolonged response latencies for congruent / incongruent prime-target pairs. Affective priming has typically been associated with spreading activation models in network-like memory structures such as semantic networks. For instance, priming of lexical decisions tasks (word / non-word judgements) suggest that priming stimuli that are related to the target preactivate parts of the representation of the target, and thus lead to faster identification of the target string as a word, if it is a word.

Early and Automatic Affective Processes as the Source of Affective Priming Effects with brief SOA of below 300ms

Affective priming effects have reliably been shown over a variety of different stimuli and response tasks. Words, names of familiar attituded objects, “Turkish words” that had only previously been learned, black-and-white line drawings, pictures, sounds and even odors have served as priming stimuli. Object naming, lexical decision and valence categorization for instance have served as response tasks. And evaluative adjectives, nouns and photographs have served as target stimuli (Fazio, 2001). Affective priming effects have been well established as automatic and distinct from later, more conscious and effortful processing. It has often been found with brief stimulus onset asynchronies (SOA) of under 300ms, but to eventually disappear with longer SOA of 1000ms (e.g. Lane, Reiman, Bradley, Lang, P.J., Ahern, Davidson, & Schwartz, 1997; DeHouwer et al., 1998; Fazio et al. 1998, 2001; Hermans et al.; 1994). A recent parametric time curve analysis of SOA in an evaluative categorization and a pronunciation task found a similar pattern, in which affective priming effects occurred only at SOA below 300ms (Hermans, DeHouwer and Eelen, 2001), and even disappeared at SOA of 450ms. If the effect were

conscious, one would expect priming effects to get enhanced rather than to evaporate when participants are given more time to evaluate the valence of the prime. Thus, this suggests that affective priming is automatic rather than due to conscious processes. Also, it has been argued that brief SOA below 300ms are too short to allow influence of conscious strategies on affective priming; which would require SOA of 500ms and more (Fazio et al., 1986). Furthermore, affective priming effects have even been found for subliminal presentation of the priming stimuli (e.g. Greenwald, Klinger, and Schuh, 1995; Winkielman, Zajonc, Schwarz, 1997, Wittenbrink, Judd, & Park, 1997, Hermas, Spruyt, De Houwer, Eelen, 2003). Thus, automatic affective priming effects are taken to be independent from later priming effects that occur with SOA above 300ms, such as repetition priming, semantic priming, semantic incongruence priming, or effects due to the stimuli format (Windman, Daum, and Güntürkün, 2002).

The automated nature of affective priming also holds with a recently proposed alternative explanation. De Houwer, Hermans, Rothermund and Wentura (2002) suggested stroop-like response conflicts or facilitations as alternative to spreading activation models as responsible mechanism for the affective priming effect. In their study, affective priming was only significant when participants rated targets based on valence but not when they rated them based on their semantic category. Hence, they argue that “[...] affective priming is due to processes that occur at the response selection stage rather than to processes that occur at the semantic encoding stage [...]”, such that congruent primes activate the same response pathway as the target response, resulting in a faster response. Incongruent primes on the other hand pre-activate response pathways different from the target response, leading to stroop-like response conflicts and prolonged reaction times. However, as Fazio (2001) correctly points out, both the spreading activation and the response conflict explanations of affective priming involve the activation of automatic affect evaluations as the “same initial step” (p. 120). Hence, under both accounts we can expect to be able to elicit affective priming effects in hemineglect.

Conclusion

In sum, we hypothesize that hemineglect patients should be able to process residual visual information, even if they can not consciously report having seen them. We try to show residual visual processing in neglect with means of an indirect test. That is, we think the affective priming

paradigm is such an indirect test suitable to assess residual processing abilities in hemineglect. This is because with a SOA between prime and target of below 300 ms we can expect to elicit early and automatic affect processing, and because we take early levels of affect processing as a promising candidate to demonstrate residual affective processing of visual stimuli in hemineglect.

Experimental Design and Procedure

Participants

Participants were 52 students of the University of Osnabrück. 27 were male, 25 were female. Each subject had a normal or corrected to normal vision.

Materials

The program runs on a Acer Notebook, the Display is a 17" Acer TFT-Monitor. The interaction is carried out through a standard mouse.

The presented pictures were selected from the International Affective Picture System [Lang et.al. 1995] based on normative pleasure ratings to produce three 30-item sets each of positive, neutral and negative pictures. Pleasant pictures included themes such as babies, sports events, etc. Unpleasant pictures included themes such as frightening animals, human violence, etc. Neutral pictures consisted of inanimate objects, people with neutral facial expressions and complex visual stimuli (e.g. scenes, patterns, etc.). These three sets were the prime pictures. Additional 80 (90%) neutral pictures were selected as target pictures. 5 positive and 5 negative pictures (10%) were added to suppress a neutral rating bias.

Procedure

The subjects are advised about the evaluation task by the program. They were told, that the aim of the experiment was to investigate the influence of disturbance on the evaluation of pictures. The exact procedure of the experiment was explained to them.

The subjects place their chin on a chinrest so that they can fixate on the screen easily 50 cm away from the screen. In the beginning of the experiment the subject saw a fixation cross in the middle of the screen. In each trial the fixation cross was presented for 500 ms. Then a prime picture was presented for 200 ms in either the left or the right visual field. The centre of the

prime picture was placed 7° away from the centre, so that it was presented completely only in one visual field. The vertical angle was 9,33° due to the fact, that the pictures should not overlap. The calculations resulted from a picture size of 10,95 cm times 8,22 cm on the screen. 50ms after the prime the target picture is presented in the middle of the screen. The subjects had to rate the target pictures on a 9-point-Likert-scale, from -4 (very unpleasant) to +4, (very pleasant) . The target pictures consisted of 90% neutral and 5% each positive and negative pictures. Only the neutral target pictures were relevant for the analysis, the positive and negative pictures are added to the test to reduce a bias in the subjects.

The evaluation task is self timed, when the subject selected a value on the scale the next trial starts automatically. Each subjects rated 90 target pictures.

Before the test itself there were ten trial runs, after the trail runs ended, there was shown information, that the main test begins.

Researching Affect with Pictures and Ratings Scales

We used photographs from the International Affective Picture System (IAPS) both as primes and as targets of the affective priming experiments, and a 9-point Likert rating scale as measure of affective valence. This choice of stimuli and measurement entails some commitment to assumptions on the nature of emotion and affect and how it can be measured. The main purpose of this section is to review the validation of IAPS picture ratings against other measures of emotion, both conceptually and experimentally. Thus, this section begins with Lang, Bradley and Cuthbert's (1998) derivation of emotional measures from evolutionary theories of emotion, than reports experimental results with physiological and behavioural measures of emotion, and ends with validating the IAPS pictures against these measurements. If not otherwise stated, what is presented here is based on a comprehensive review article by Lang et al. (1998).

Evolutionary theory of Emotion

Lang et al. take both an evolutionary, and an action perspective on emotion. They take an action perspective, because they conceptualize emotions as “motivationally tuned states of readiness” (Lang et al, 1998, p347). They take an evolutionary perspective, because they argue that these states of readiness are derived from primitive actions that ensured survival in evolutionary processes. In this line of reasoning, Lang et al. argue that the numerous emotional

expressions that results from the numerous ways of possible actions can be characterized by their motivational basis in terms of two evolutionary plausible dimensions: approach and withdrawal responses. Primitive actions like unconditioned responses for instance seem organized to either preserve a state (like sex, joy, or nurturance), or to protect the organism (like fear or anger). Both has evolutionary advantage: emotions signalling withdrawal behaviour the will lead to avoidance of dangerous situations, whereas emotions signalling approaching behaviour lead to an active exploration of new environments.

Such a conceptualization is not uncommon. In a similar spirit are models of distinct behavioral systems for approach and withdrawal which through the course of learning lead to two repertoires of physiological responses and perceptual-motor patterns. Again, these two systems serve as motivations for a two-dimensional description of affective states in terms of approach and withdrawal. Such a two-dimensional categorization of affective expressions has even been observed in language. Affective descriptors can be classified as a distribution over a bipolar dimension from negative to positive affect.

Measures of Emotion

As the above conception of emotion as “states of readiness” is tightly coupled to actions, so are measures of emotion tightly coupled to action. Emotion has been measured essentially on three levels. On a physiological level in terms of responses of the somatic and autonomic system to emotional stimuli, such as facial muscle activity, heart rate, or skin conductance. On a behavioral level in terms of action patterns such as, for instance, the startle reflex on first exposure, or choice viewing times of emotional stimuli. On a conscious level in terms of language use as the observed variable. Yet, this broad range of data produces substantial noise, and poses difficulties in theoretically interpreting the results of studies on emotion. Correlations between emotional parameters for instance often are rather modest, and emotional responses may vary within subjects across different contexts of stimulation. Given these obstacles, the more surprising it is that similar patterns of data on emotional processing could be found between these levels.

Means of Emotion Elicitation

One issue in studies of emotional processing is to find suitable stimuli to evoke emotion. Over the years, standardized stimuli sets have been constructed for instance with pictures, e.g. the International Affective Pictures System by Lang et al. (1995), with sounds, e.g. the collection of International Affective Digitized Sounds by Bradley, Cuthbert, and Lang (1998a), and with words, e.g. the collection of Affective Norms for English Words by Bradley, Cuthbert and Lang (1998). For a review see also the Handbook of Emotion Elicitation and Assessment by Coan and Allen (forthcoming).

Concerning picture stimuli, Lang et al. (1998) argue that emotion induction by pictures has the particular advantage of reduced motor activity. Often physiological correlates serve as emotional measures, and motor activity is a major input to physiological responses. In a picture viewing paradigm it is of advantage that motor activity is reduced, and thus physiological responses observed are largely those of perception and emotional motivation.

The International Affective Picture System and the SAM Rating Scale of Emotional Valence

The International Affective Picture System (IAPS) that we used in the affective priming experiment is a set of 600 standardized pictures developed by Lang et al. (1995) for studies on emotion. It consists “of a large array of color slides depicting a range of objects and situations that vary in interest value and pleasantness, including pictures of household utensils, food, plants, animals, landscapes, children and adults, vehicles, weapons, natural disasters, and erotica” (Patrick, 1997, p298. Lang et al. calibrated the pictures with the ratings of approximately 400 participants using the Self-Assessment Manikin (Bradley and Lang, 1994), a rating scale with the dimensions affective valence and arousal. The dimension valence and arousal are not independent, but give a boomerang shape when plotted against each other, such that pictures rated as calm and non-affective on the valence scale were also rated low in arousal, and pictures rated as highly affective, either negative or positive, were also rated as more arousing. This seems to be a stable pattern, as it was also found for ratings of sounds and english words.

Factor analysis of ratings on the SAM scale in fact reveals negative and positive affect as possible underlying dimensions. This espoused attempts to assess emotion on orthogonal dimensions for negative and positive valence, rather than with valence and arousal. Yet, in a

study contrasting ratings of the same pictures in both rating systems, Patrick and Lavoro (1997) obtained inconsistent results. Ratings for unpleasant pictures were higher rated on the negative dimension as expected, but unexpectedly also systematically rated higher on the positive dimension as the negative ratings increased. As a result, SAM scale with valence and arousal are the commonly used scales in ratings of emotion.

Validation of IAPS Picture Ratings

IAPS ratings have been validated against a physiological and behavioural emotional measures. As physiological correlates of IAPS ratings, fascial muscle activity and heart rate increase both with valence and arousal. Skin conductance goes up, and slow cortical responses in EEG becomes more positive with increase in arousal ratings, but not with valence ratings. As behavioral measures, for instance reaction times on first exposure are longer for pictures with more extreme valence rating, probably because emotional pictures gain more attention. In choice viewing behaviour, when people are allowed to look freely at the images, they spend more time on pictures with higher affective ratings, except in phobia conditions where the stimuli can evoke considerable distress and provoke avoidance behaviour.³ Correlations also systematically map onto the valence and arousal dimensions. Factorial analysis of ratings, physiological and behavioral measurements of emotional states evoked by means of IAPS pictures reveals two factors which seem to represent the arousal and valence domain. Pleasantness ratings, heart rate and fascial muscles activity load onto the factor supposedly representing valence, arousal and interest ratings, viewing time, skin conductance and slow-wave EEG data load onto the factor supposedly representing arousal. This means that ratings of IAPS pictures are in line with more direct physiological and behavioral measures of emotion.

Second Research Interest: Lateralization of Emotional Processing

The prolonged delay in obtaining permission for patient experiments by the ethics committee made it likely that we might not get permission to test patients within the one-year period of the project (see the section on the ethics review in part IV.1). As a response to this, we prepared an experimental hypothesis on the lateralization of emotional processing that can be studied with the

³ Yet, these relational patterns in emotional measure can vary between individuals, and between particular groups like e.g. gender groups.

current paradigm in a student population. This hypothesis is broadly described below. More details and experimental results are given in the stand-alone paper on affective priming (part II.2).

Research on hemispheric specialization in emotional processing shows a variety of inconsistent results, which lead to inconsistent models of lateralization of emotional processing (for reviews see e.g. Canli, 1999; Davidson, 1995). Part of the data on emotional lateralization supports the right-hemisphere hypothesis (e.g. Borod, 1992), according to which the right hemisphere is in general more specialized for emotional processing than the left hemisphere. Part of the data support a first valence hypothesis, according to which emotional processing is lateralized by valence. It assumes larger involvement of the right hemisphere in positive emotion and larger involvement of the left hemisphere in negative emotion (e.g. Davidson, 1984). Other data supports a second valence hypothesis that supposes the opposite pattern, that is, larger involvement of the right hemisphere in the processing of negative emotions, and larger involvement of the left hemisphere in the processing of positive emotion (e.g. Canli, Desmond, Zaho, Glover, Gabrieli, 1998; Bolte, Goschke, & Kuhl, 2003).

Versace et al. (in revision) suggest a possible reason for these opposing theories on emotional lateralization is that they take data from a diverse number of paradigms as their input, so that multiple processes involved in hemispheric asymmetries are likely to be confounded in the observed data. Models of emotional processing e.g. have taken data across brain imaging, EEG recordings and patient data, among others, as their basis. The opposing results of studies on emotional lateralization might come about because effects found in different paradigms might be due to different processes involved in emotional functions. Thus, Versace et al. point out the need to isolate more clearly the various processes that lead to the observed hemispheric asymmetries in emotion.

Conclusion

In this second study, we aimed to demonstrate lateralized negative and positive priming effects that follow one of the theories on emotional lateralization within a student population. Since the lateralized affective priming paradigm described above in part was designed to isolate early automatic affective valence evaluations from later affective processes, found

lateralization effects would selectively describe affect lateralization at this early level of processing. Experimental results of this experiment are reported in the stand-alone paper (part II.2).

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Appendix A: IAPS images

positive	negative	neutral	neutral
1440	1040	1450	7150 *
1460	1280	1600	7170
1710	1300	1670	7190
1750	1301	1740	7207
1920	1930	1810	7217
1999	2900	1910	7224
2070	3180	2190	7233
2080	3300	2200	7234
2092	3550	2260	7235 *
2170	6260	2410	7490
2340	6510	2590	7500
2501	9120	2840	7510
2620	9140	4100	7550 *
4653	9270	5010	7620
5480	9300	5020	7700
5626	9421	5250	7710 *
5629	9560	5500 *	7830
5760	9570	5510	7900
5910	9800	5520	9070
7580	9810	5530	9090
8500	1040	5531	9210
1722	1070	5532 *	2514
1850	1300	5533 *	2570
1942	2205	5534	2575
2057	2750	5731	2830
2616	3181	5870	2870
5831	3230	5891	2880
8461	3350	5991	2890
8497	3530	6150	5390
8503	3550	7000	5740
	6560	7002	7004
	6570	7006	7020
	9041	7009	7185
	9280	7010 *	7186
	9584	7025	7205
	9800	7030	
	9910	7034 *	
		7035	
		7040	
		7060 *	
		7080	
		7090	
		7100	
		7130 *	
		7140	

Pictures marked with * were used twice, once in their original form and once mirrored.

Automatic affective processing in the left and right hemisphere has qualitative influence on conscious perception of affective valence

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Abstract

Automatic processing of affect has frequently been proposed to influence further cognitive processing and conscious perception. This study aimed to show an influence of automatic affect processing on explicit, conscious perception of the emotional valence. In an affective priming paradigm with affective pictures, we aimed to show a qualitative rating bias in conscious emotional ratings of target stimuli that were preceded by negative or positive primes. That is, we aimed to show changes in the qualitative content of the target response due to automatic affective processing of the prime. A negative priming effect could be demonstrated in form of a negative rating bias for target pictures with negative primes. This indicates that automatic affect processing has influence on the qualitative content of later conscious processing, as is often predicted. As a secondary goal, this study aimed to investigate hemispheric asymmetries in automatic affect processing using lateralized presentation of primes. No difference in priming effects for left and right visual field presentation was found. Both methodological considerations concerning the lateralization procedure, as well as a theoretical interpretation of the absence of lateralization effects in automatic affect processing are discussed as explanations.

Introduction

Automatic processing of the affective valence of a stimulus has been suggested within emotional theories for about two decades (e.g. Zajonc, 1980, 1984). Affective states have frequently been conceptualized as physiological and motivational “states of readiness” for primitive actions towards aversive or appetitive stimuli (e.g. Lang, Bradley

and Cuthbert, 1998, p397). Such states bias the actions of an organisms towards aversive or appetitive behaviour, to either avoid or to explore its environment (e.g. Davidson & Irwin, 1999). *Automatic* activation especially of negative affect in response to dangerous environmental stimuli is likely to have evolutionary advantage, allowing the organisms to avoid danger based on fast and automatic processing without the need for time consuming conscious recollection. Therefore, early and automatic affective processes are thought to shape behaviour and later cognitive processing. Such an impact of automatic processing of affect has been discussed in areas such as for instance social psychology (e.g. Zajonc, 1980, 1984), learning theory (e.g. Martin & Levey, 1978) and personality psychology (e.g. Kuhl, 2000). To give one example, automatic affect processing is thought to influence the ease of decision making by reducing cognitive demands (Blascovich et al., 1993; Fazio, Blascovich, & Driscoll, 1992).

To investigate the characteristics of automatic affective processing and its influence on later cognitive processes, affective priming is recently being used intensively (DeHouwer and Hermans, 2001). The affective priming effect has been investigated in a number of experiments that manipulated the affective relation between prime and target pairs (for a review see Fazio, 2001).

In these studies, the the affective priming effect has been well established as automatic. It has often been found to occur with brief stimulus onset asynchronies (SOA) of under 300ms, but to eventually disappear with longer SOA of 1000ms (e.g. Lane, Reiman, Bradley, Lang, P.J., Ahern, Davidson, & Schwartz, 1997; DeHouwer et al., 1998; Fazio et al. 1986; Hermans et al.; 1994). A recent parametric time curve analysis of SOA in an evaluative categorization and a pronunciation task found a similar pattern, in which affective priming occurred only at SOA below 300ms

(Hermans, DeHouwer and Eelen, 2001), and even disappeared at SOA of 450ms. This has been taken to suggest that the affective priming effect is automatic rather than due to conscious processes. If it were conscious, one would expect priming effects to get enhanced rather than to evaporate when participants are given more time to evaluate the valence of the prime (Fazio, 2001). Also, it has been argued that brief SOA below 300ms are too short to allow influence of conscious strategies on affective priming; which would require SOA of 500ms and more (Fazio et al., 1986). Furthermore, affective priming effects have even been found for subliminal presentation of the priming stimuli (e.g. Winkielman, Zajonc, Schwarz, 1997; Hermans, Spruyt, DeHouwer, and Eelen, 2003). Thus, automatic affective priming effects are taken to be independent from later priming effects that occur with SOA above 300ms, such as repetition priming, semantic priming, semantic incongruence priming, or effects due to the stimuli format (Windman, Daum, and Güntürkün, 2002).

The affective priming effect has also been established to be general. It was found for a broad variety of stimuli including words (e.g. Fazio et al., 1986; Hermans et al., 1994), nonsense words whose meanings had only previously been learned (DeHouwer, Hermans and Eelen, 1998), line drawings (e.g. in Hermans, DeHouwer and Eelen, 2001), pictures (e.g. Fazio, 1993; Hermans et al., 1994) and odours (Hermans, Baeyens, Eelen, 1998). It was also found with different kinds of response tasks, including evaluative valence categorization (e.g. Bergh et al., 1992; Fazio et al., 1986), traditional lexical decision (e.g. Kemp-Wheeler and Hill, 1992; Hermans; Wentura, 1998), word identification (e.g. in Fazio, 2001), and pronunciation (e.g. Hermans et al. 1994).

Many of these studies use differences in response latencies as the measure for the influence of the prime on the target task. Reaction time measures assess if automatic affective processing of the prime leads to faster responses to the target when the target is affectively congruent to the prime. However, reaction time measures can not assess if automatic affective processing of the valence of the prime also changes the content of a target task qualitatively, as predicted by the theories of automatic affect processing (e.g. Zajonc, 1980, 1984).

In the present study, we aimed to demonstrate that automatic affect processing has qualitative influence on explicit, conscious perception. That is, we aimed to show an affective priming effect on the content of conscious evaluations of the affective valence of target pictures. We used standardized pictures from the International Affective Picture System by Lang et al. (1995) both as prime and target stimuli. To reliably evoke early and automated rather than later and more effortful affective evaluation processes, we used a brief stimulus onset asynchrony of 250ms between prime and target. Primes had negative, positive or neutral valence, and participants were asked to evaluate the affective valence of neutral target pictures. Common valence evaluation tasks ask participants to classify target stimuli in negative, neutral and positive categories, and use differences in response latencies as the measure of priming effects. By contrast, the valence evaluation task used here asked for emotional ratings on a valence dimension in order to show a qualitative effect on the content of the target evaluation. Participants should rate the affective valence of neutral target pictures on a 9-point Likert scale from 'very unpleasant' to 'very pleasant'. We expected to find rating biases on the target pictures as the measure of priming effects, so that neutral targets preceded by negative primes get rated more negatively than neutral targets preceded by positive primes, and vice versa.

Lateralization of Affect

Since automatic affect processing is well-established as source of affective priming effects, therefore, affective priming paradigms may be used to investigate the characteristics of automatic processing of affect. In a second research interest that is not directly related to the above we address one characteristic of automatic processing of affect: its hemispheric lateralization.

Research on hemispheric specialization in emotional processing shows a variety of inconsistent results, which lead to inconsistent models of lateralization of emotional processing (for reviews see e.g. Canli, 1999; Davidson, 1995). Part of the data on emotional lateralization supports the 'right-hemisphere hypothesis' (e.g. Borod, 1992), according to which the right hemisphere in general is more specialized for

emotional processing than the left hemisphere. Part of the data support a first ‘valence hypothesis’, according to which emotional processing is lateralized by valence. It assumes larger involvement of the right hemisphere in positive emotion and larger involvement of the left hemisphere in negative emotion (e.g. Davidson, 1984). Part of the data support a second valence hypothesis that supposes the opposite pattern, that is, larger involvement of the right hemisphere in the processing of negative emotions, and larger involvement of the left hemisphere in the processing of positive emotion (e.g. Canli, Desmond, Zaho, Glover, Gabrieli, 1998; Bolte, Goschke, & Kuhl, 2003).

With means of lateralized presentation of the priming stimuli, we aim to evoke automatic affect processing separately in each hemisphere. Thus, we can discriminate what influence automatic affect processing originating in either the left or the right hemisphere has on a response task towards centrally displayed target stimuli. If automatic processing of affect is lateralized, observed priming effects should follow one of the theories on emotional lateralization. Should automatic affect processing be lateralized according to the right-hemisphere hypothesis, we expected to find stronger priming effects both for negative and positive primes when presented to the right hemisphere. However, should automatic affect processing be lateralized according to the first valence-hypothesis, we expected to find stronger effects for negative prime when presented to the right hemisphere, that is the left visual hemi-field, and stronger effects for positive primes when presented to the left hemisphere, that is, the right visual hemi-field. Should automatic affect processing be lateralized according to the second valence hypothesis, we expected to find the opposite pattern.

Methods

Participants

A total of 52 subjects, 27 male, 25 female with a mean age of 22,54 (SD 2,46) participated. All subjects had normal or corrected to normal vision.

Materials

All stimuli were taken from the International Affective Picture System by Lang, Bradley and Cuthbert (1995). Stimuli were categorized according to valence of the pictures as negative, positive, and neutral. Since the IAPS did not provide enough neutral stimuli, 11 neutral pictures (11%) were used twice, but horizontally flipped. The priming stimuli had 30 pictures each in these categories. The target set had 90 pictures, of which the majority of 80 pictures (90%) had neutral valence. Additionally, 5 negative and 5 positive pictures (10%) were included as filler items to suppress a neutral ratings bias.

The experimental program was written in Borland Delphi 5.0, using a high-precision timer with a resolution of 1 ms. Pictures were presented on a 17” colour TFT display.

Procedure

Participants were instructed that the aim of the experiment was to investigate the influence of distraction on emotional ratings of pictures. They were asked to give valence ratings on pictures, and to fixate on the fixation mark, ignoring eventually upcoming distracters.

In total, the experiment had 90 trials, of which five were probe trials. Each trial started with a fixation mark shown for 500 ms, randomly followed by a negative, neutral or positive prime for 200ms. Then, 50ms after the prime disappeared, a target picture appeared (of which 90% were neutral, and only 10% of the targets randomly were negative or positive). Together with the target, also a 9 point Likert scale from unpleasant (-4) to pleasant (+4) appeared, and was shown until the participants gave their rating. That is, the evaluation task was self-timed, with the next trial starting automatically after a rating was given.

Subjects had to rest their head on a chin rest, such that their eyes had a distance of 50cm to the screen. The presentation of the priming pictures was lateralized, that is, they were randomly presented 7° to the left or right from the centre of the display, in order to project them in separate halves of the visual field (Tootell, Mendola, Hadjikhani, Liu and Dale, 1998). The vertical angle of the primes was 9.33°, so that prime and

target pictures did not overlap. Both primes and targets had a size of 10,95 cm x 8,22 cm as displayed on the screen. The target pictures were displayed in the middle of the screen and thus presented to both halves of the visual field. The Likert scale was presented as a line of radio boxes below the target picture, denoting the ends of the scale as very unpleasant and very pleasant, respectively. No box was preselected, and ratings were given with a mouse.

Results

Only ratings of neutral targets were of interest and went into analysis. Data from 6 participants had to be excluded from analysis due to data recording errors (3), or because participants did not properly fixate on the fixation mark (3), so that data of 46 participants was analysed. All analyses were done with $\alpha = .05$.

A 3x2 repeated measure ANOVA with valence (negative, positive, neutral) as first and presentation side (left, right) as second factor showed a main effect for the valence of the prime, $F(1,4)=9.14$; $p=.001$, but no interaction between valence and presentation side was found.

Post-hoc t-tests showed targets with negative primes ($M_{neg}=0.09$, $SD=.79$) were rated more negative than targets with neutral primes ($M_{neut}=0.50$; $SD=0.77$, $t(45)=3.1$; $p=.03$). However, ratings of targets with positive primes ($M_{pos}=0.55$), did not differ from targets with neutral primes. No difference due to lateralization was found for negative primes and positive primes. However, for neutral primes, left visual field presentation lead to more positive target ratings ($M_{neut_left}=0.62$), and right visual field presentation lead to more negative ($M_{neut_right}=0.38$) target ratings ($M_{diff_neut}=0.24$; $SD= 0.69$; $t(45)=2.3$; $p =.025$). But with a Bonferroni corrected significance level of $p(0.05/3)=0.016$, this difference was not significant.

Discussion and Conclusion

Our findings demonstrate a quantitative influence of automatic affect processing on explicit, conscious perception of the valence of

later stimuli. Conscious evaluations of target pictures showed a negative rating bias if they were preceded by negatively connotated primes. No rating bias for positive priming pictures was found. In a secondary question of the same experiment, we did not find hemispheric differences in affective priming due to lateralized presentation of the priming stimuli. However, our results may give suggestive evidence for an lateralization effect with neutral primes, though the effect was not significant after Bonferroni correction of the significance level.

Early affect processing influences conscious valence perception

Concerning our main research question, our findings indicate that automatic affective processes that occur in affective priming with brief SOA can have qualitative influence on later, conscious processing, in addition to their influence on response latencies. This finding is in line with Fazio's (e.g. 2001) model of automatic attitude/valence activation as explanation of affective priming. Fazio's models suggests that affective attitudes towards a prime are automatically retrieved from memory, and, by spreading activation, pre-activate attitudes towards affectively congruent targets. This reduces the activation threshold of the target task for affectively congruent targets, which leads to faster response latencies. A plausible explanation for the present findings is that negative primes selectively pre-activate possible negative attitudes of target pictures, reducing their activation threshold, and thus giving them an advantage over possible positive attitudes toward the same target in later conscious processing. As a result, the overall evaluation task processing is biased in its qualitative content towards the valence of the prime. This demonstrates that automatic affective processing has qualitative influence on later cognitive processing, as it is often predicted (e.g. Zajonc, 1980, 1984).

Fazio's model also predicts a positive priming effect, which could not be shown in the present study. However, in the literature positive priming has frequently been reported to be less reliable than negative priming, and automatic processing especially of negative affect has been assumed to have evolutionary advantage (e.g. in Vuilleumier

and Schwartz, 2001). It might thus be that our paradigm could detect a large negative priming effect, but is not sensitive enough for positive priming effects of smaller size. In particular, participants might have adopted a neutral rating bias as cognitive strategy due to the fact that the large majority of targets was neutral (even though we added 10% filler items with positive and negative affect in prevention). If it was present, such a neutral rating likely was not strong enough to override all effects, as demonstrated by the found negative priming effect. Yet, it might have been large enough to override possible positive priming effects, if those are smaller in size than negative priming effects.

There is one serious restriction in the above interpretation of our results. Because our paradigm used changes in the content of the target task rather than changes in response latencies as measure for priming effects, a single study can not establish the found effect to be due to the influence of automatic affective processing of the prime on the conscious target task. This is because with a presentation time of 200ms, participants can consciously perceive the primes. Thus it is possible that the found effect is due to conscious processing of the prime, rather than due to automatic affect processes. But, it seems unlikely that the effect could be completely due to conscious processes. Due to their automatic nature, affective processes as found in the research program of Fazio (e.g. 2001) can be expected to be responsible at least in part. If automatic affect processes, as we propose, have a major or the complete share in priming of conscious valence evaluation, then systematic manipulation of SOA should replicate the findings with different SOA that have been done with target tasks using reaction time as measure of priming (e.g. Hermans, DeHouwer and Eelen, 2001). Increasing SOA should lead the effect to disappear, and, also, subliminal presentation of the primes should not.

Lateralization of automatic affect processing

Concerning our second research interest, we did not find an interaction between the valence of the primes and the visual semi-field they were presented to. One possible reason is that the lateralization procedure employed might not have

ensured presentation of the primes into visual field halves. Although subjects were instructed to fixate on the fixation mark until the target appeared, this might not have been enough to suppress automatic orientation responses towards the primes when they appeared (e.g. Wentura, Rothermund and Bak, 2000). This is especially true for negative primes, as negative stimuli seem to have an evolutionary advantage in attracting attention towards the space where the negative stimuli appear (e.g. Vuilleumier and Schwartz, 2001). Yet, a weak argument indicating that the lateralization procedure did work in our experiment is given by the fact that we found a difference due to lateralized presentation for neutral primes, though this difference was not significant after Bonferroni correction. Improvements of the paradigm might try to replace the constant fixation cross with a slightly changing (e.g. colour and form) or a moving fixation mark, so as to attract more attention towards the fixation mark.

A second possible explanation for the absence of an interaction between valence and lateralization is that our study had only medium statistical power to detect it. Lateralization effects in affective priming can be expected to be relatively small. Both valence hypotheses and also the right hemisphere hypothesis equally predict lateralization effects not as a 'direct' priming effect, but as a more 'indirect' difference only in the size of the priming effects in the left and the right hemisphere. The first valence hypothesis for instance predicts positive priming only to be larger in the left than in the right hemisphere, but does not predict it to occur exclusively in one hemisphere. Such a difference in size can be expected to be smaller than the absolute size of the priming effects it results from. A post-hoc analysis of the effect size confirms this expectation. The interaction between valence and hemi had a small effect size of partial $\eta^2=0.05$. Post-hoc analysis of power revealed a power of 0.45 for an interaction effect of this size. This means that we had a probability of 45% to detect a lateralization effect, if it was there, and a probability of 65% to commit a beta error. (By contrast, for the main effect of valence we gained a power of 0.92 for the effect size of part. $\eta^2=0.169$).

With such a medium power, a theoretical interpretation of the absence of an effect can only

be accepted with reservation. Yet, one theoretical assumption explaining the absence of lateralization effects is that emotional processes may not be lateralized at the early and automatic stages of processing we aimed to test. Rather, lateralization might occur only at later stages of emotional processing. This view gets support by a recent finding on lateralized affective priming effects. Versace et al. (in revision) found a negative priming effect for targets presented to the left visual field, that is, to the right hemisphere, and a positive priming effect for targets presented to the right visual field, that is, to the left hemisphere. However, contrary to our experiment, Versace et al. lateralized the target pictures rather than the primes, and therefore did not evoke automatic affect processes separately in each hemisphere. Thus, it is possible that their results do not reflect lateralization of early automatic affective processing, as investigated in this experiment with lateralized presentation of the prime. Rather, Versace et al. may have found lateralization of emotional processes at later stages, which lead to hemispheric differences in how sensitive the target task is for the influence of the prime.

Concerning the indication of lateralization differences for neutral primes, one possible explanation were a baseline difference in automatic affect processing between the hemispheres. Primes might be evaluated more positive by left-hemispheric automatic affect processes than by automatic processes in the right hemisphere. However, such a baseline difference may not be strong enough to substantially influence highly emotional priming stimuli (either negative or positive) in a significant manner, so that the baseline might show only with neutral primes.

Conclusion

In conclusion, automatic affective processing not accelerates or delays the processing of later cognitive tasks, as it is often found in affective priming research. Rather, our main finding shows that automatic affective processing also has qualitative influence on the content of later cognitive processing. This gives further support to the affective primacy hypothesis, stating that early and automatic affect processes prime later cognitive processing. The present findings might

also suggest that lateralization of emotional processing occurs not at early and automatic, but at later stages of emotional processing. Yet, for this interpretation two improvements seem in need. First, it is necessary to show that the lateralization procedure correctly presents the primes into the visual semi-fields. Second, higher statistical power is required for a meaningful theoretical interpretation of the absence of lateralization effects.

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Part III

Spatial navigation & Hippocampus

Theoretical Background of Spatial Navigation

Neural Correlates, Sex Differences and Virtual Reality

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1. Introduction

The second line of interest of the project was similarly twofold as the first. On one side we were interested in the neural correlates of spatial representations and processes, specifically those in the medial temporal lobes, on the other side we wanted to investigate sex differences in the realm of spatial navigation. While the former scope was tightly connected to the study of spatial behavior in neurological patients and preredquired a collaboration with the neurological clinic similar to the investigation of patients suffering hemineglect, the latter was based on behavioral differences between genders in a normal population.

This part of the documentation will therefore introduce the reader to the research area of spatial navigation, including a short discussion of the theoretical background of spatial representations and resulting strategies, a review of relevant literature regarding the neural correlates of spatial knowledge and of behavioral differences between men and women, and finally a discussion of methodological issues – specifically of the use of virtual reality tools to investigate spatial navigation in humans.

After reading this part of the documentation the reader will have a broad idea about the area of spatial navigation in general, and a more concise understanding of the specific background and the motivation of our experiments.

2. Theoretical Issues of Spatial Navigation

The domain of spatial navigation is interested in how one deals with the omnipresent challenges the 3-dimensional, spatial world that we live and move in gives us every day. Specifically, questions as “How do we find our way in new or known places?”, “How do we acquire the knowledge necessary to find back to a place that we visited before?” or as “How is spatial knowledge represented in the brain?” are in the scope of this field.

We were especially interested in the navigational ability of human subjects in unknown environments and in the neural basis of this ability. We had the possibility to use an implementation of the virtual Morris water maze to investigate the domain. The use of this paradigm has two main advantages. Firstly, the original (not-virtual) Morris water task (Morris, 1981) was used in this area of research with animals, specifically rodents, for more than 20 years

and therefore it is possible to draw information from the literature. Secondly, experimenting with subjects in virtual environments enables researchers to assess spatial behavior in a new quality with greater control of the experimental conditions and less costs. Later we will deal with the advantages and limitations of the application of virtual environment methodologies in more detail.

2.1 The Morris water task (MWT)

The MWT is a paradigm that enables the study of spatial behavior in a relatively small and simple environment, the Morris water maze (MWM). The MWM is a circular pool filled with opaque water and equipped with an escape platform that has to be reached and climbed to escape the uncomfortably wet environment (Fig. 1).



Figure 1. A Morris water maze filled with opaque water (<http://www.bol.ucla.edu>).

The idea is to observe the development of spatial behavior of the subject in goal-finding and to infer thereby on which basis space is navigated. There are two basic distinctions to make regarding the goal-finding condition within the paradigm (Morris, 1981). The design of the experiment can be divided in “proximal” and “distal” localization of a goal, an escape platform. In a “proximal” localization task the goal would be visible itself or its position would be signaled by a nearby visible cue, for example a light bulb hanging over the goal, or some other sensory

detectable means as smell or acoustic cues. Learning of the task in this condition demands “only” a sensory sensitivity towards the cue, which has to be associated with the goal, and a motor “taxi” system that allows moving towards it. The “distal” localization task, on the other hand, requires a more elaborated navigation system, as no nearby cues mark the location of the goal. Here the goal is “hidden” and orientation towards it is only possible by making use of distal cues, as for example objects in the environment. A representation of the relation between the environmental cues and the goal has to be built. As our interest is directed towards this latter kind of spatial representation we use the “hidden platform” version of the MWT. Subjects are exposed to the virtual pool, which is located in a quadratic room with distinguishable visual cues on the four walls. The platform itself cannot be seen and only by a random search strategy it is possible to encounter it the first time. However, after the platform is found the subject is again “dropped” into the pool, this time in a different start location.

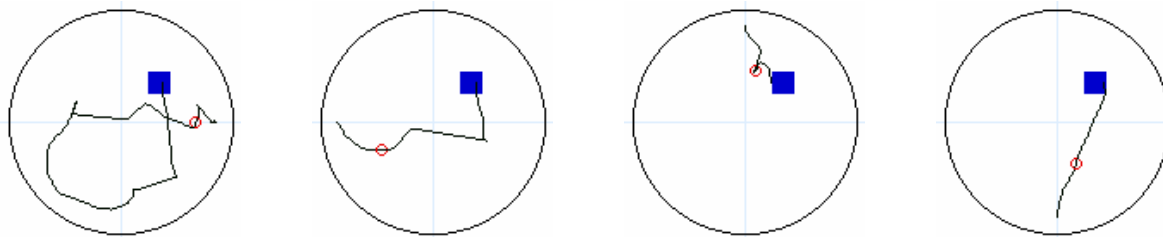


Figure 2. Four successive example trials from the virtual MWT showing continuous place learning from trial to trial. Though the start location is changing from trial to trial, the subject acquires an increasingly accurate representation of the platform position.

This assures that there is no possibility to find the platform just by conducting the same motor program, but rather forces the subject to make use of the distal cues to find the goal again. Thus, to perform successfully the subject has to encode the platform location in relation to the distal cues, as proximal or geometric cues are essentially missing (see Fig. 2).

The spatial information that is obtained by experience in unknown environments can be represented in two spatial frameworks, an egocentric and an allocentric one (Burgess et al., 2002). This division is important and the next section will clarify the basic differences between both frameworks of spatial representation.

2.2 Representations of spatial knowledge

When we navigate through unknown environments we automatically build up representations of them, some do more efficiently and others do less. These representations capture the

information we encounter in form of spatial layouts of environments, object positions and spatial relations between the objects encountered. As we are moving through these environments with our body, which is the carrier of the sensory systems perceiving the objects, borders, and obstacles surrounding us, the first representation(s) of the environment are built relative to our body. This is referred to as egocentric representation.

The more we are exposed to an environment, the more information we can obtain about the locations of objects within it and the spatial relations (e.g. paths) between these objects. It is assumed, that the subject encodes this information in an allocentric representation, a so-called “cognitive map”.

While an egocentric representation of the environment would be centered relative to the body of the navigator, that is for example on head or trunk of the subjects, an allocentric representation would be fixed on environmental features, such as the geometric shape of it and/or the position of objects within it. As a consequence egocentric representations are very movement sensitive. The representation changes with every movement because every movement would change the relation between the subject and the environmental cues. The allocentric representation, on the other hand, remains stable, as a movement changes only the position of the subject within the fixed set of (spatially) related cues.

2.3 Strategies in spatial navigation

Redish (1999) enumerates several strategies to solve spatial tasks, which can be divided along the egocentric/allocentric distinction: Egocentric strategies are random navigation, taxon navigation, praxic navigation, and route navigation. Random navigation is used when no sufficient information about the environment and the goal is available, and the subject has therefore to rely on random search. In taxon navigation a cue has to be present towards which the subject can move to approach the goal. Praxic navigation is the use of a fixed motor program to reach the goal, as for example a certain number of steps into a known direction. Finally, for route navigation an association of a direction with each sensory view is necessary, so that a chaining of sequences of taxon and praxic substrategies can lead to the goal.

Redish identifies locale navigation as allocentric strategy in which the subject is learning a map on which the goal is represented in relation to other cues. Knowledge of the location of the goal and the own position on this map enables the subject to plan a path to the goal.

Another important characteristic of cognitive maps is their flexibility. In allocentric representations, the viewer can instantiate his position in any relation to various visible cues and the goal, while in egocentric representation, this is not possible for views the subject did not experience before. The environmental features (as for example landmarks) are always stored in relation to the viewer himself. If a subject has never been in a certain position, it cannot access egocentric knowledge never encountered from this position.

While in principle most navigation tasks can be solved by egocentric strategies, there is evidence from electrophysiological studies in rats and humans for the existence of allocentric representations.

3. The Hippocampus – A Neural Correlate of Spatial Navigation?

3.1 Identifying the hippocampal function in spatial navigation

While egocentric representations are supposed to be correlated with parietal areas (Colby & Goldberg, 1999), allocentric representations are associated with activation in the hippocampal formation (Fig. 3B). Though the validity of a distinction between ego- and allocentric representation is doubted by several researchers (Shelton & McNamara, 2001; but see McNamara et al., 2003), there is growing evidence for the existence of allocentric representations and its location in the hippocampal formation.

Tolman (1948) was the first who proposed the existence of a cognitive map in rats. 30 years later O'Keefe and Nadel (1978) published in their seminal work "The Hippocampus as a Cognitive Map" the modern cognitive map theory. Here, on the basis of the discovery of viewpoint-independent, place-coding cells in the rat hippocampus by O'Keefe and Dostrovsky (1971), the hippocampus became the purported host of an allocentric representation.

Later studies revealed other brain structures adjacent to the hippocampus are also involved in spatial cognition: For example, in the postsubiculum (PoS, also known as dorsal presubiculum), another structure in the hippocampal formation, direction sensitive cells were found by Ranck et al, 1984. Head direction cells are neurons that encode the direction the head is facing, irrespective of where the animal is in the environment. Together head-direction and place cells are supposed to build the neural substrate for an allocentric representation.

The importance of the hippocampus in spatial memory was also shown in lesion studies, where rats with lesioned hippocampus were impaired in tasks of spatial navigation where no proximal cues indicated the target position, as in the Morris water maze. While normal rats learned the location of a target over trials, lesioned rats searched randomly without showing signs of spatial knowledge acquisition (Mumby et al., 1999; Sutherland et al., 1982; Morris, 1982).

A principal problem in the analysis of hippocampal function in humans is the limited access to single cell recordings. Ekstrom (2004) obtained single cell and EEG recordings from epileptic patients assessed for resection planning, and showed thereby the existence of hippocampal cells that responded on specific spatial locations and without a preference for a direction of view, reminiscent of those found in the rat hippocampus. However, while for rats the involvement of both hippocampi in spatial navigation seems clear, studies on human spatial navigation are less unanimous. Though there is a broad consensus that the hippocampus is a key structure in memory (Squire & Zola-Morgan, 1991), there is debate about a possible functional lateralization of the structure, with the left hippocampus mainly involved in verbal memory, and the right hippocampus in spatial memory.

Imaging studies in the domain of spatial navigation showed that right hippocampal activation correlated with the accuracy of way-finding in virtual environments (Maguire et al., 1998; Grön et al., 2000; Hartley et al., 2003), suggesting a relation between allocentric representation use and navigational accuracy. However there was also activation of the left hippocampus, but as it was not correlated with navigational accuracy it is rather interpreted as non-geometrical memory function. A problem of the interpretation of functional imaging studies is the limited ability to differentiate between functional necessary activation and incidental coactivation of a structure. Therefore studies of patients that suffered damage to those structures can supplement our understanding of their involvement in spatial navigation.

Patient studies examining the effect of unilateral hippocampal damage show in general lateralization of spatial memory function to the right part of the structure (Jones-Gotman, 1997; Pigott & Milner, 1993; Jones-Gotman, 1986; Smith & Milner, 1981; Corkin, 1965), while verbal memory is mainly affected by damage to the left part. Impairments following right hippocampal damage are as manifold as object-location tasks, memorizing visual scenes, learning of abstract designs and maze navigation tasks.

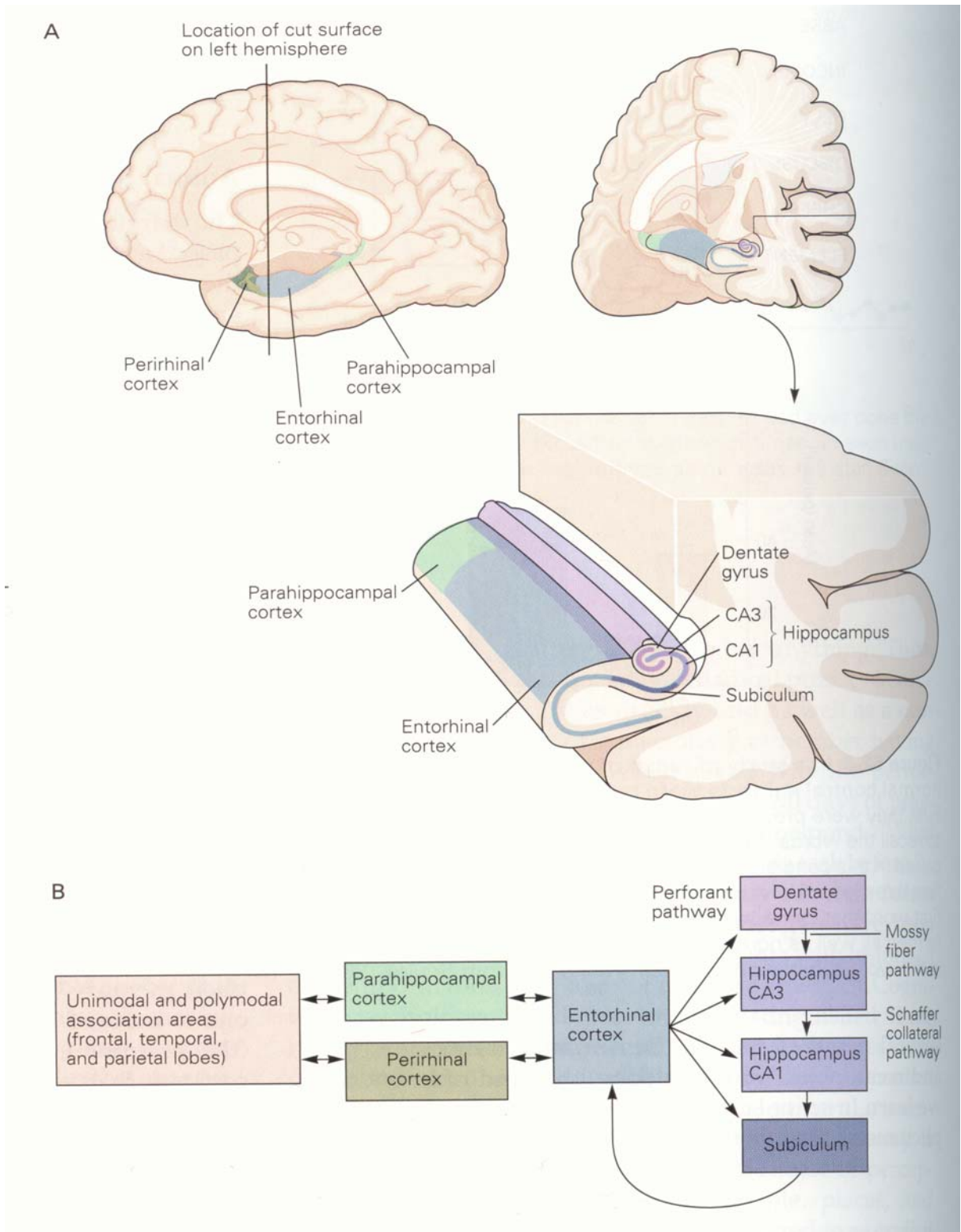


Figure 3. The Hippocampus and adjacent structures involved in spatial memory (Kandel et al., 2000).

Bohbot et al. (1998) studied besides others a group of patients with damage in the hippocampus. They found that patients with right hippocampal damage performed worse in spatial memory tasks, whereas patients with left hippocampal damage were mainly impaired in verbal memory tasks. Interestingly, they found patients with hippocampal damage unimpaired in a 30 minutes delay task similar to the Morris water task, whereas patients with damage to the right parahippocampal cortex showed impairment in the task. The interpretation of these results can be aided by imaging studies. Consistently with other imaging studies, Burgess et al. (2002) identified this structure as a part of the human navigation system. Specifically they claimed that the right parahippocampal cortex plays an important role in representing the geometry of spatial scenes (see also Epstein et al., 2003; Epstein & Kanwisher, 1998), “whether or not this is used in memory”. Evidence for a role of the structure in spatial memory based on an egocentric reference frame comes from a patient study examining spatial memory with a delayed oculomotor response task (Ploner et al., 2000). Therefore this structure constitutes a communication link between the egocentric and allocentric representations consistent with its function as main structure connecting parietal areas with the hippocampus (Mishkin et al., 1999, see also Fig. 3B), but might also in itself pose an important instance in the memorization of (egocentric) spatial information. Assuming this, the finding of Bohbot et al. might be explained by an involuntary tapping of spatial ability based on a parahippocampus-dependent egocentric representation rather than on a hippocampus-dependent allocentric representation.⁴

Consistent with this interpretation a patient study on a virtual Morris water task revealed severe impairment for patients that underwent either amygdalohippocampectomy (which reduces the surgical damage done to the overlying cortices, i.e. parahippocampal cortex) or anterior temporal lobectomy (in which the overlying cortices are necessarily damaged) for the cure of medically intractable epilepsy (Astur et al., 2002). Thereby it made no difference if the patients suffered loss of the left or right hippocampus, indicating the necessity of both structures in a navigation task assumed to foster, if not require the use of allocentric representations. These results are contradictory to the former findings that the hippocampal functions are lateralized and only the right part is essential for spatial navigation. To shed more light on this issue, we want to

⁴ The “invisible sensor task” employed by Bohbot et al. differed from the original Morris water task by the lack of a probe trial and of the measurement of navigation speed, which offers alternative interpretation for their findings (Astur et al., 2002).

conduct the following experiment that resembles the one of Astur et al.. While our primary aim is the replication of this study, our hope is to examine the performance of patients who suffered a damage more circumscribed to only hippocampal areas.

3.2 Experimental Design

To probe if left or right hippocampal damage have different effects on the navigational abilities patients have to absolve the “distal” localization task in the Morris water task described above. The subject has to find a hidden platform in a water pool. As soon as the platform is found there is a 5 seconds long pause, which can and should be used to orient in the room. If the subject does not find the platform within 60 seconds it will appear automatically and the subject is commanded to “swim” towards it. While searching and after the platform is found the distal cues pose the only means of orientation in an otherwise uniform environment. As distal cues we use familiar objects, like a window, bookshelf, poster and door. The platform will always be at the same place in the pool, but starting positions will be randomly assigned for each trial. After 20 practice trials a probe trial of 30 sec is applied which apparently resembles the practice trials with the difference that there is no platform in the pool. The probe trial is thought to reveal if the subjects have acquired a “spatial strategy”, an idea of where (in which quadrant) to search for the platform. After 30 seconds the probe trial ends automatically. Thereafter this 20 practice trials and another probe trial will be repeated. Besides the two groups of hippocampal patients (left and right unilateral) we additionally will test a control group of patients who have had operations on the spinal cord. As dependent variables measures of trial latency (the time needed to locate the platform), heading error (the deviation from a direct heading of the subject towards the platform position), path length and spatial strategy (percentage of the path length that the subject spent in the quadrant where the platform was located in the practice trials).

3.3 Hypotheses

If the spatial function of the hippocampus is mainly restricted to its right part, we would expect that patients that suffered damage to the right hippocampus perform significantly worse than those that suffered damage to the left hippocampus. While latter patients should perform somewhat equal to a control group without cerebral lesions, the former should exhibit greater problems in the task than the control patients. Contrariwise, if both hippocampi are necessary for

the acquisition and use of spatial knowledge, there should be no significant difference between both patient groups, but a significantly worse performance when they are compared to the control group. However, it has to be noted that an implication of both hippocampi in spatial navigation is not automatically giving evidence that both are involved in the formation and use of an allocentric representations. It could be still possible that the right hippocampus is serving mainly spatial memory, whereas the left hippocampus is supporting a verbal strategy to memorize the platform position. The optimal (unimpaired) performance may than just be achieved by combining both sources of information.

4. Sex Differences In Spatial Navigation

Many studies have already investigated the differences between the genders in regard to spatial abilities. Male superiority in performance for navigation tasks has been shown with rats in real mazes (Roof, 1993; Williams & Meck, 1991) as well as with humans in virtual environments (Astur et al., 1998).

In particular, it has been found for humans (similar as it was shown for rats) that the genders differ in their use of cues: Whereas men use both geometric cues and landmarks, women prefer the use of landmarks only (Sandstrom et al., 1998). These findings already suggest that males and females do not use the same navigational strategies, in particular that women tend to use landmarks to build up an egocentric representation of their environment to find their way, whereas men rather build up cognitive maps with information about angles and distance. Grön et al. (2000) showed in an imaging study in humans performing a navigation task that the hippocampus was more activated for males than for females, whereas the parietal cortex showed more activation for females than males. Assuming the neuronal basis of allocentric representations in the hippocampal formation and of egocentric representations in the parietal cortices (see section 3.1) these outcomes are concordant with the findings and interpretations cited above. Altogether, this is evidence that women and men tend to use different cue types (i.e., geometrical or distal cues) to form different types of representation (allocentric or egocentric) processed in different regions in the brain (hippocampus or parietal lobe). Therefore we believe that the gender difference in performance in spatial navigation tasks as the Morris water maze used by Astur et al. (1998) arises from navigational strategies based on differential representations.

Another Morris water maze study has shown that men and women are influenced in different ways by interleaved blocks of trials where the platform is located at unexpected places. In this condition, women were less affected compared to men (Derek A. Hamilton, personal communication). Using an classical Morris water task employing only distal cues (see section 2.1) with interleaved blocks in which the platform changed from block to block, the aim of our experiment was twofold. Firstly, we wanted to replicate the general sex difference mentioned above, expressed by shorter swimming latencies for male subjects compared to female subjects. Secondly, we wanted to investigate the influence the interleaved non-stationary platform trials have on this sex difference, specifically if this sex difference in navigation, expressed by different swimming latencies, disappears or reverses when the first trials of the stationary blocks between men and women are compared. Thereby we hoped to gain more insights about the nature of the sex difference in spatial navigation. The methodological details, results and a comprehensive discussion of them can be found in the paper (*“A vanishing sex difference in the latency to learn the position of a hidden platform in the Morris water maze”*).

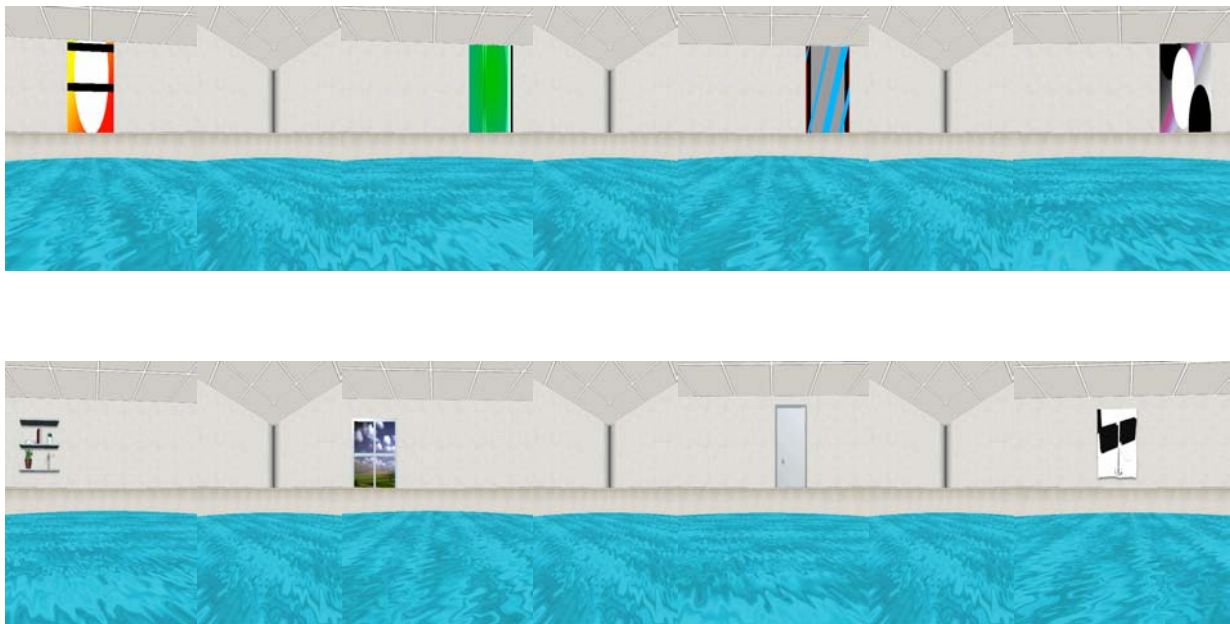


Figure 4. A wide-view of the environment of the virtual Morris water task. The upper wide-view (constructed from several 60° views) contains abstract distal cues, while the lower is showing a maze with everyday objects as distal cues.

5. Cognitive Assessment and Virtual Reality⁵

5.1 What is virtual reality?

A general definition would describe virtual reality (VR) as “a way for humans to visualize, manipulate, and interact with computers and extremely complex data”. For our purposes we might constrain this definition towards a more concrete version: “VR can be viewed as a user interface designed to ‘interact’ and become ‘immersed’ with an computer-generated environment”. Popular examples therefore are airplane simulators. By their complexity and resemblance to the real-world environment and situation they allow a dynamical training and the assessment of pilots in situations otherwise to costly or risky to train. There are multiple ways of output imaginable, from simple monitors to 3D head-mounted displays and surround sound, as there are also manifold possibilities to use input devices, from joystick, mouse, or keyboard, to data gloves and voice controllers. Indeed there is even the possibility to mediate tactile sensations by “force feedback” mechanisms (air bladders, micropins or mechanical exoskeletons). By this multitude of technical devices the deliberate simulation of complex scenarios has become possible to a degree where the difference to real-world scenarios might be reduced to an astonishing degree. Still this is only the beginning.

And it is by this virtue of simulating real-world situations that VR becomes interesting for the psychological sciences as cognitive and neuropsychology. The aims of this disciplines are manifold and reach from the support in “determining a diagnosis [and] provision of normative information on the status of cognitive and functional abilities [over] producing guidelines for the design of rehabilitative strategies [towards the creation of] data for the scientific understanding of brain function” and cognitive processes. To achieve this aims effective methods and instruments of cognitive assessment are necessary. But most of the traditional methodology, especially those assessing higher cognitive functions, due to the necessity to be administered in a controlled environment, lack ecological validity and are often highly contrived. This may be one of the most fundamental problems of experimental psychology. The increasing availability and quality of VR technologies, combined with the decreasing costs of hardware, will enable psychologists to overcome these problems. Before we will discuss the advantages and

⁵ If not indicated otherwise the information of this chapter is taken from Rizzo & Buckwalter (1998).

possibilities, but also the limitations of the new technology, a short introduction to the history of psychology and its research instruments will give a clearer picture of how VR is supposed to support research.

5.2 A short history of research instruments⁶

In the end of the 19th century the scientific approach towards the human mind took its beginning, developing out of philosophy and up to this point mainly relying on introspection and speculation. The new empirical approach towards the mind was aided by the experimental method, which supported, inspired and constrained the theorizing. In the center of this approach stands the inference of cognitive processes from the measurement of behavior towards certain stimuli.

Out of the research field of physiology came the instruments which enabled the high precision, by controlling variations in stimulus presentation and the registration and measurement of responses, which was necessary to generate reliable findings. Between the instruments controlling stimulus presentation were the “color mixer (for varying wave length composition and/or brightness of a visual stimulus), aesthesiometer (for varying tactile stimuli), the accoumeter (for varying amplitude of sound), and the tonometer (for varying frequency of sound), while precise response registration was supported by instruments such as the kymograph (which allowed analogue registration of a continuous response), the cardiograph (for heart rate), the plethysmograph (for pulse), the ergograph (for effort expended and fatigue), and the chronoscope”. Those instruments were soon found as the standard fixtures of every psychological laboratory. Other, more specialized apparatus were soon created to study higher and more complex mental processes, as for example the “memory apparatus” of Georg Elias Myller, the “larynx sound recorder” Felix Krueger, Karl Marbe’s apparatus for the melody of speech, or Emil Kraepelin’s “writing apparatus”.

In the midst of the 20th century then the informatics revolution brought computers into the laboratories, first only as means of gathering and processing the experimental data. Later they became more and more involved in the whole experimental process, from the presentation of the stimuli to the recording of the responses. It is in this line of steady development that VR technologies became involved in psychological research in the last decade.

⁶ The information of the history section, if not indicated otherwise, can be found in Gaggioli (2003).

However, it has to be mentioned that from the first appearance of VR technology to the experimental use of it some decades had to pass. The first VR application was an installation of Morton Heilig in 1962 called “Sensorama”. This motorcycle simulator allowed a ride through New York with fan-generated wind and typical smells, and though the route was pre-recorded and therefore without any possibility for interaction it had all the other characteristics of a VR system. Ivan Sutherland, a pioneer of computer graphics, a few years thereafter constructed the first head mounted displays, with stereoscopic vision, computer-generated (vs. recorded) visual images and the user’s view determined by his head’s movements. In the 70’s then the already above mentioned flight simulators were realized and in the 80’s the VIVED project (Virtual Visual Environment Display) and later the VIEW project (Virtual Interactive Environment Workstation) were developing user interfaces to aid the natural interaction with large-scale autonomous integrated systems. In the last decade then the development of faster computers enabled interactivity to a high degree. This and advanced visualization software made a broad range of VR applications in education, medicine, industry, military training and entertainment possible. And here experimental psychologists began to take interest in this new technology as one more instrument to explore the vast and resistant white patches upon the map of the human mind.

5.3 Advantages and limitations of VR in psychological experimenting

This new technology is offering new possibilities to the scientific community interested in cognitive processes. But as every existent technology it has its specific limitations that have to be well studied to assure the reliability and validity of the new methods coming with it. This section will deal with general advantages and limitations of the use of VR in psychology, before we come to the specific research field of spatial navigation and the application of VR-based experiments in this domain.

Two criteria have to be satisfyingly fulfilled to judge a measurement useful for psychology, reliability and validity. Reliability is the ”capacity of an instrument to consistently obtain the same results”. Validity is, “how well an instrument measures what it purports to measure.” Traditional experimental methods, such as those conducted with paper and pencil, have to face problems with both of these criteria.

Reliability is dependent on a multitude of factors, as the examiner conducting the experiment (especially if there has to be a steady interaction), the environment the experiment is done in (light, sound, etc.), and the quality of material (the stimuli) the experiment is using. By using VR environments it is possible to present stimuli in a more controlled, systematic way, and thereby to cancel out some of those negative influences. However, to reach an optimal reliability of VR methods, reference standards have to be created for those VR methods, which can lead scientists in the development and usage of them, as subtle differences in VR environments may obtain different results in the same tasks.

Similarly, validity can be improved by the use of VR. With all aspects of observable behavior of the subject steadily controlled and continuously recorded by the computer, an amount and quality of discrete data is available, that is unlikely to be delivered by traditional methods, as for example observers (however well-trained they might be). This allows the deconstruction of complex behavior along the subtle lines of subprocesses making it up. It is by this virtue that, by the use of appropriate analytic techniques, complex cognitive constructs can be reduced to a multitude of specific cognitive constructs, which supports the increase of validity of the measurement. On the other hand, the increasing amount of data produced in this experiments has to be handled with care, for otherwise the scientist may drown in it.

Psychological experiments have always to be balanced between a controlled situation in which the causalities of the observed behavior are clearly assignable and interfering factors can be excluded, and situations that are most similar to the real world with all its complexity and unpredictability. This balance between controlled simplicity and “ecological validity” becomes increasingly difficult the higher the cognitive mechanisms that are to be studied are. More complex and dynamic experimental environments are needed to observe behavior that is also relevant in real-world situations. With VR environments this balance may be kept easier, as the experimenter has the control over all aspects of the environmental situation, however complex it might be. Instead of relying on data from contrived testing environments, behavior can be observed in scenarios closely resembling real-world situations. Of course, it is also here that an obvious advantage has to be met with care, as the design of artificial worlds itself can never in all aspects resemble the real world. Though the technology is continuously advancing, there are and presumably will be obvious differences between studies conducted in natural and in VR environments. Despite the magnificent developments of visual and acoustical interfaces and

software, other sensory aspects as touch and smell are less well substitutable by now. Similarly, ideothetic information, proprioception and the vestibular sense, cannot be manipulated artificially by now. A way to ensure that this lack of realism is not affecting the validity of the measurements is to look if the knowledge or abilities acquired in VR are transferred to real environments and real-world situations. This can be referred to as “generalization”.

5.4 VR and the research on human spatial navigation

After this general introduction of VR in cognitive assessment, and before we evaluate the virtual environment we use, we will shortly consider VR in the context of spatial navigation research. As already mentioned VR enables us to study the behavior of subjects in complex environments otherwise hard to control. For spatial navigation one of the main advantages is obviously that subjects can be tested in environments (for example buildings or landscapes) that are either not available or whose construction in the real-world would not be affordable. Additionally, most computer systems can be carried and installed everywhere, whereas subjects, and especially patients with neurological disorders, may not be that flexible.

However, there are some issues that experimenters have to bear in mind when planning VR experiments. In VR environments no self-motion is experienced besides the one necessary to use the controls that allow for movement in the virtual world. Therefore only minimal sensorimotor feedback is available. This seems especially important in studies exploring navigational behavior, as studies in mammals showed that ideothetic information is similarly prominent as visual information in building abstract representations of the environment (McNaughton et al., 1996). Concordant with this fact Gaunet et al. (2001) showed that active exploration of an virtual environment is enhancing spatial memory performance less than that of an real environment, compared to passive exploration (as for example by viewing a video or snapshots). The difference between virtual and real-world condition may be attributed to the visual dominance of VR tasks, arising out of the lack of ideothetic information. In this context it is also important to note, that the visual characteristics of objects (for example distal or proximal landmarks) play a prominent role in the virtual environment. As those objects are the anchors of the spatial representations built up (see section 2.1), their memorizability is significantly influencing performance (Ruddle et al., 1997).

Furthermore, dependent on the kind of VR system used the prior experience with computers and especially the prior experience 3D computer-generated worlds may affect performance. The more natural the control interface is (keyboard- vs. stepper or bicycling-controlled movement), and the more holistic the “virtual illusion” is (achieved for example by the use of head mounted displays), the less differences in previous exposure of the subjects to computers or artificial 3D worlds will matter. Connected to this issue is also the concept of “immersion” or “presence” (Held & Durlach, 1992, in Maguire et al., 1999). The more realistic a virtual environment is designed, the more a subject immerses in it, that is the subject feels a stronger presence of the virtual environment. Witmer and Singer (1994, in Maguire et al., 1999) found that the feeling of presence and performance in the virtual environment are significantly correlating. In this sense experience with 3D virtual worlds may promote a feeling of presence when those experienced subjects have to perform a VR experiment, while inexperienced subjects need a certain time to accommodate to the unusual interaction with a virtual world.

However, as mentioned in the previous section, generalization of the knowledge acquired in VR is indicating that the processes that are involved in the exploration of virtual environments and in performing a task therein are similar to those utilized in real environments. For the domain of spatial navigation this transfer effects were found in several studies (Ruddle et al., 1997; Goldberg, 1994; Johnson, 1994) suggesting that in deed comparable mental representations are built.

5.5 The virtual Morris water task

In the last 8 years a small but considerable amount of studies employing the virtual Morris water maze as the method to investigate behavioral characteristics and neural correlates of human spatial navigation was generated. Thereby a multitude of results revealed similar spatial behavior of human subjects as it was observed for rodents.

Jacobs et al. (1997) showed that the latency to find the platform is decreasing from trial to trial, showing that a mental representation of the platform location is built as it is done by rodents solving the task (Morris, 1981). Therein distal cues are integrated, irrespectively if proximal cues are available for use or not. A similar finding for rats was presented by Cressant et al. (1997). Jacobs et al. (1998) examined the relation between cues used in the task and revealed that subsets of distal cues that were available when the target location was learned are sufficient to perform

the task (in the rodent literature: Fenton et al., 1994), while changes in the distal cue order are disrupting place learning (in the rodent literature: Pico et al., 1985; Suzuki et al., 1980; O'Keefe & Conway, 1978). Furthermore there is evidence from human and rodent studies that the hippocampus is of crucial importance in the performance of the Morris water task (Astur et al., 2002; Mumby et al., 1999, respectively). And finally similar sex differences were observed in human VR mazes (Astur et al., 1998; Sandstrom et al., 1998) as in experiments with rats (Perrot-Sinal et al., 1996).

These findings indicated that the mechanisms of spatial navigation in humans, especially those of spatial knowledge acquisition, are in principle equivalent to those postulated and confirmed for rodents. Moreover this concordance observed between human and rodent studies generally speaks in favor for the usability of virtual paradigms in the cognitive assessment of human navigational behavior, and specifically for the validity of the virtual Morris water task.

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A vanishing sex difference in the latency to learn the position of a hidden platform in the Morris water maze

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Abstract

Sex differences are frequently found in the domain of spatial navigation, generally of the sort that males are superior in their performance than females, independent of the species studied. One study (Astur et al., 1998) using the paradigm of the virtual Morris water task revealed a large and reliable sex difference between human subjects. To further investigate this difference we chose a classical Morris water task but inserted a block with non-stationary platform location after every stationary platform block. While we observed the expected sex difference, we found that the interleaved non-stationary blocks reduce the performance difference between the genders, indicating that women were less affected than men by the interleaved non-stationary blocks. This can be taken as evidence that women and men are using differential strategies, based on egocentric and allocentric representations respectively, to perform the Morris water task. This is in line with studies indicating differential preferences and abilities to use distal or geometrical cues, and differential brain activations of men and women in navigation tasks.

Introduction

Many studies explore the influence of gender on spatial ability in manifold ways: men perform better than women in mental rotation tasks (Tapley & Briden, 1977), the Piagetan water level task (Goodrich et al., 1993), way-finding (Lawton,

1994), route learning (Galea & Kimura, 1993) and direction-giving (Ward et al., 1986).

The current study deals with sex differences in spatial navigation in the Morris water task, specifically with the influence that interleaved non-stationary target location trials have on the performance in a classical platform learning paradigm with a stationary target location.

In examining past studies it is easy to see, that the concept of spatial abilities is a broad one and the tasks vary in their requirements and in the processes involved. They can be divided into navigational and non-navigational spatial abilities. In our experiment we focused on the former ones. As a standard measure for spatial navigation in rodents, mazes like the Morris water maze (Morris, 1981), the Hebb-Williams maze (Hebb & Williams, 1946) or corridor mazes have been used for over 30 years.

The recent development of virtual reality environments makes the assessment of navigational abilities in humans in similar settings, under similar parameters possible. Furthermore, although studies with actual mazes have been conducted (Bohbot et al., 1994; Kállai et al. 1995), the usage of virtual environments allows a tighter control of the experimental conditions and a better assessment of the performance. Investigations with human subjects in different kinds of virtual mazes have produced similar results as seen in non-virtual rodent studies, for example the acquisition of spatial knowledge (Jackobs et al. 1997), the importance of distal cues (Jacobs et al., 1998), and the crucial involvement of hippocampal structures (Astur et al., 2002). Specifically there is evidence for a sex difference in navigational ability in

virtual reality mazes (Morris water maze: Sandstrom et al., 1998; Astur et al., 1998; Hebb-Williams maze: Shore et al., 2001) as it was also shown for rodents (Perrot-Sinal et al., 1996; Roof, 1993; Williams & Meck, 1991).

We chose for our purposes the Morris water maze (Morris, 1981). In the Morris water task the subject has to find a platform in a circular pool situated in a quadratic room. The platform is hidden and there are no proximal cues within the pool that could indicate the platform location. Around the pool at the walls of the room, distal cues are arranged. To perform successfully the subject has to encode the platform location in relation to the distal cues, as proximal or geometric cues are essentially missing.

Astur et al. (1998) showed in various experiments a reliable sex difference in the virtual Morris water task. Participants had to escape from a virtual pool by finding a hidden platform over 20 trials after which a probe trial without platform was to be performed. Over all these experiments in which the position of the target did not change, the participants showed continual increase of their performance to locate the platform, that is, the swimming latency decreased. Overall, men were faster in finding the hidden platform, made smaller heading errors and showed a better spatial strategy in the probe trials⁷ compared to women. A control task with a visible platform trials indicated that the sex difference was not the result of motivational, motor or sensory differences regarding the computer program, rather it could be traced back to navigational ability. This sex difference has been interpreted as a possible consequence of social pressures, different hormone levels, or different preferential strategies formed in the course of evolution (see Astur et al., 1998 for references).

In our experiment we wanted to investigate the influence interleaved non-stationary platform trials have on the performance of men and women, that is on the previously mentioned sex differences. For this purpose, subjects had to perform a Morris water maze task similar to those of the Astur et al.

study with an interleaved non-stationary platform block after each stationary platform block. While the platform location did not change over the stationary platform blocks, it was randomly assigned to a different location for each non-stationary platform block. Stationary and non-stationary blocks differed also in the distal cue design, with every-day cues (window, shelf, picture, door) and abstract cues (4 abstract pictures) randomly and evenly distributed over men and women.

We chose the second environment to be without predictable platform location over blocks but predictable (stationary) within blocks to maximize the confusion about the platform location, but in the same time to minimize the probability that subject just conceptualize the non-stationary platform blocks as totally random (which would have been the case in a trial to trial randomization). The former should make sure that subjects do not learn one general platform location for all interleaved blocks, but for each block have to learn a new location. The latter should ensure that subjects still use some kind of navigation strategy other than random navigation.

If the interleaved non-stationary blocks have an influence on the performance in the stationary blocks it should mainly be revealed in the first trial of each stationary block preceded by a non-stationary block. Other studies using the same design have shown that men and women are influenced in different ways by the interleaved non-stationary blocks, with women less affected compared to men (Derek A. Hamilton, personal communication).

The aim of the current experiment is twofold. Firstly, we want to replicate the general sex difference mentioned above, expressed by shorter swimming latencies and smaller heading errors for male subjects compared to female subjects. Secondly, we want to investigate the influence interleaved non-stationary platform trials have on this sex difference, specifically if this sex difference in navigation, expressed by different swimming latencies, disappears or reverses when the first trials of the stationary blocks between men and women are compared.

⁷ The term spatial strategy refers to the percentage of the path length that the subject spent in the quadrant where the platform was located in the practice trials. A successful spatial strategy required the subject to spend more than 40% of the path length in the target quadrant.

Methods

Participants

We tested 46 students, 23 male students and 23 female students, from the human sciences department. The mean age was 23 (respectively, 23.3 for the males and 22.7 for the females). As compensation they received course credits for their study or took part in a lotto with the chance to win 50 €.

Techniques

We used an implementation of a virtual Morris water task of the Neuroinvestigations, Inc.. The experiments were done on an IBM-compatible computer with a Pentium III 800MHz processor, 256 MB RAM, a 32 MB RAM ATI Graphics Card and standard input devices (an IBM-compatible keyboard). The image was displayed on a 17" monitor with a resolution 1280 x 1024 (16 Mio. colors, 85 Hz refresh).

Design

The experiment consisted of 14 blocks, 7 of the stationary platform conditions and 7 of the non-stationary platform condition, with 4 trials building each block. The blocks of the two conditions were alternating, beginning with a stationary platform condition block. While in the stationary platform condition the platform was tied to the same location within the pool over all blocks, in the non-stationary platform condition the location was randomly reassigned for each block. Within the blocks of both conditions the platform was located at the same place over the 4 trials. However, the starting position within the pool was randomly determined for each trial. The two conditions used different sets of distal cues (abstract objects: colorful abstract pictures vs. familiar every day objects: window, bookshelf, poster, door) which made it possible for the subject to discriminate between the conditions, though nothing was told about the stationary/non-stationary platform design. The association of the cue types with the condition type (abstracts – stationary/familiar – non-stationary vs. abstract –

non-stationary/familiar – stationary) was randomly and evenly distributed over the subjects.

Procedure

After reading an information sheet with general instructions concerning the experiment (basically finding the hidden platform), participants had to give their informed consent. Thereafter they were instructed to navigate in the virtual 3D surrounding with the help of the arrow keys (forward, right, left) of the keyboard and to use the distal cues to orient. Furthermore the participants were told that after 60 seconds inefficient search the platform would appear. It was emphasized to use the 5 seconds remaining to the next trial after the platform was discovered to turn and orient in the room, as it could be helpful to find it again in the next trial. There was a 60° field of egocentric view of the virtual space, which is approximately the same as the human eye. Every 100 ms the position of the subject was recorded in the form of x,y coordinates. The latency and path length to locate the platform were determined from this data. The heading error was determined after the subject traveled a path length $\frac{1}{4}$ of the pool diameter, or if the platform was found before this point immediately before the subject stepped on the platform.

Results

A repeated measure ANOVA with the swimming latency of all stationary trials as 28 step between-factor revealed a main effect of group (gender), $F(1, 44) = 10.19, P < .001$.

Furthermore a significant difference was observed for the within-factor trial, $F(27,1188) = 7.29, P < .001$. A comparison of the means of the first and the last trial was also significant with $t(90) = 6.49, P < .001$, showing that the between-factor effect was caused by decreasing trial latency over the 28 trials.

When we examined the latencies in all first trials of stationary platform blocks, using repeated measure ANOVA with the 7 first trials as repeating factor, we found no main effect of group, $F(1,44) = 3.02, P > .05$. However, a between-factor effect of trial could be observed, $F(6, 264) = 7.87, P < 0.01$, and again was shown

to be caused by an decrease in latency over the blocks, $t(90) = 3.27$, $P = .002$.

To ensure that the finding of a significant main effect of group in the repeated measure ANOVA above was not precluded by the shrunken sample size we conducted the same ANOVA for all second stable trials. A significant main effect of group was observed, $F(1,44) = 9.44$, $P < .01$.

Discussion

As we predicted on the basis of other studies, a large sex difference was observed with men performing the Morris water maze better than women. Specifically men were significantly faster than women in finding the hidden platform and showed a strong trend towards a significantly smaller heading error (Fig. 1).

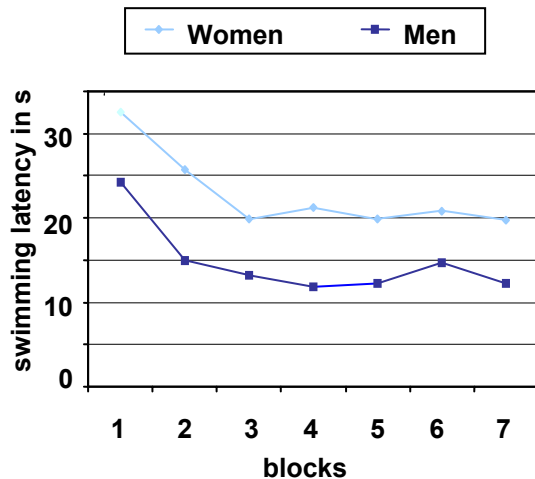


Figure 1. Development of the performance over stationary platform blocks expressed in swimming latency.

However, comparing the performance of the sexes in the first trials of the stationary blocks we found an effect of the interleaved non-stationary blocks. The interleaved blocks led to a decrease in swimming latency in the first stationary trial relative to the last trial of the preceding stationary block in both genders. This loss was larger for men than for women, causing the difference between the sexes to diminish and to become non-significant (Fig. 2).

One might question the ecological validity of the results, criticizing the fact that subjects only

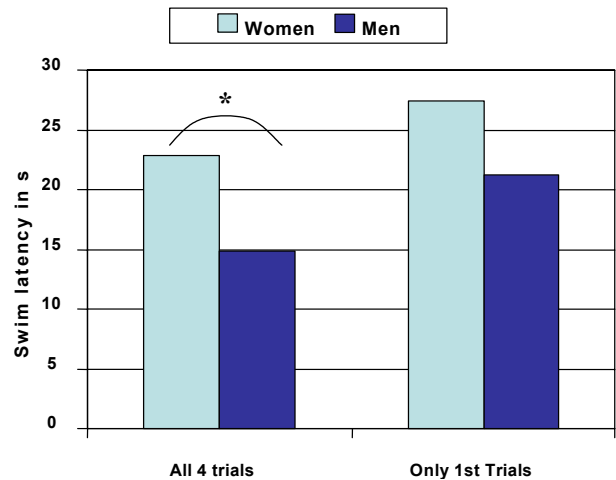


Figure 2. Mean latency to find the platform; left: performance over all four trials in the stationary blocks (* significant contrast); right: performance over just the first trials of the stationary blocks.

receive minimal proprioceptive and vestibular inputs in virtual environments. Astur et al. (2002) argue that, though vestibular information is playing a role in spatial navigation in rodents, subjects receive optokinetic information, as for example visual motion, in virtual environments, which may compensate the lack of other information. Moreover, optokinetic information alone can induce motion sickness and vertigo, which suggests that optokinetic information is interacting with the vestibular system.

In our study both sexes were deprived equally of input other than the optokinetic one. It may be possible to imagine that women and men make use of differential strategies, as we shall argument later. In this case a differential dependency on vestibular and/or proprioceptive input may be the case, producing the sex difference. However, Waller et al. (2001) compared the performance of the sexes in virtual environments and in real mazes, showing that in both differences of navigational ability can be found. This rejects the notion that the difference is merely caused by a differential dependency on vestibular or proprioceptive information.

Another point of criticism is different levels of experience with computers or computer games that might lead to the observed sex difference. Two counter-arguments address this problem: Again, the demonstration of sex differences in real-world experiments rejects the idea of a mere effect of

experience with computers. Furthermore, other studies using similar virtual environments showed that gender was the better predictor for spatial ability compared to computer experience (Shore et al., 2001; Astur et al., 1998).

A possible interpretation for the sex difference would be that men and women are initially relying on differential strategies that are based on different representations when searching for the platform. The data analysis showed that a learning process is taking place. Not only do the subjects increase their performance within stationary and non-stationary blocks, but also over the stationary blocks (Fig. 1). This indicates that the subjects are constructing and continually refining a spatial representation of the environment that is informing them about the location of the platform. There are two kinds of spatial representation, egocentric and allocentric, both theoretically useful in solving the Morris water task. To navigate through the environment subjects initially have to rely on egocentric representations, that is, on a representation of distal cues in the environment relative to the own body. By continuous exposure to the environment, it becomes possible to form relations between the various cues. An allocentric representation, a cognitive map containing information about the spatial relations between diverse distal and geometric cues and the target position is built and refined gradually, supporting the navigation process. While an egocentric representation can be used to re-establish the constellation of distal cues relative to the own body in the moment the platform was found, an allocentric representation makes it possible to derive the platform location when cues and own position within the environment are known.

Several studies indicate that it takes longer for women to establish an accurate allocentric representation, and therefore they have to rely longer on a less effective egocentric representation.

Firstly, Sandstrom et al. (1998) showed that men and women differ in the kind of cues they use in tasks of spatial navigation like the Morris water maze. While men used distal and geometric (spatial room layout) cues to find a hidden platform, women were mostly navigating with the help of distal cues. Several other studies also found that women tend to use landmarks to find their way, whereas men exhibit a preference for

information about angles and distance (Saucier et al., 2002; see ref.). Saucier et al. presented evidence, that this difference can be traced back to dimorphic capacity to use the 2 types of cues. This indicates a basic difference in the way the sexes orient in and navigate through the world, and it may be related to the use of differential representations. The preference for distal cue (landmarks) use, or the relative lack of sensitivity towards geometric cues, may cause the slower acquisition of cognitive maps and a stronger reliance on egocentric representations. Thus, men are more effective in construction and use of an allocentric representation of the environment relying on geometrical and distal cues, while women initially rely instead on an egocentric representation. This leads to an advantage of men in spatial navigation tasks.

Secondly, assuming egocentric representation to be mainly supported by parietal cortex (Colby & Goldberg, 1999), and allocentric representations by the hippocampus (O'Keefe & Nadel, 1978; Ekstrom, 2004), differential brain activations (Grön et al., 2000) indicate the use of differential representations. While performing a complex, three-dimensional virtual-reality maze, both men and women showed, besides others, strong activations in the hippocampus proper, the parahippocampal gyrus and parietal regions. This indicates that both sexes are performing on the basis of the same neural systems as outlined above. However, compatible with the differential cue use mentioned above and with the idea of different representations preferentially used, woman showed stronger activations in a right parietal area and a right prefrontal area, whereas men exhibited stronger activation in the left hippocampus.

Viewing our second result, the vanishing of the sex difference, in this light suggests that the use of differential navigational strategies, based on egocentric and allocentric representations, causes the different effects of the interleaved non-stationary blocks on performance.

We took the vanishing sex difference in the first stationary trials as an indicator that men were affected stronger than women by the change of condition, which makes them lose their general advantage in spatial navigation. An alternative interpretation would be that both men and women were affected to the same degree, resembling a

kind of initial resetting of spatial knowledge. This implies that both would lose all their spatial knowledge about the environment and be completely disoriented. It would also be expressed as a vanishing of the sex difference because the spatial knowledge of both genders would be *zero*. However, this interpretation is unlikely because the general learning curve over all first stable trials implies that there *is* some spatial knowledge that is constantly increasing from first stable trial to first stable trial by a process of learning.

So if we assume that men and women are affected to different degrees by the interleaved non-stationary blocks, what is the cause? Assuming the stronger reliance of men on allocentric representations, and of women on egocentric ones, the effect could be explained by the characteristics of these representations. For example, the general advantage of men in simple tasks of spatial navigation might turn into disadvantage when differential environments are alternating, as the cognitive maps of the two environments are interfering with each other, maybe due to an automatic process of generalization based on similar geometric cues of the two environments. Women, on the other hand, would be less affected by the change of the environment as the egocentric representation is based on the use of clearly distinguishable distal cues, and therefore it is not possible to confound the different environments.

To clarify if the vanishing sex difference is really caused by the reliance on differential representations it would be interesting to design a task, employing interleaved non-stationary blocks, that forces women to build up and work with an allocentric representation. This could be done by the manipulation of the cues necessary to orient, for example removal of the distal cues and addition of geometrical cues. If men and women are using allocentric representations to navigate the Morris water task the overall sex difference should still be found, maybe even enlarged (Sandstrom et al., 1998), but more importantly also a sex difference in the first trials of the stationary blocks.

Conclusion

The outcome of the experiment showed that interleaved blocks of a non-stationary platform condition have differential effects on the performance of men and women in the Morris water task. Though a significant overall sex difference could be observed, indicating a faster development of an accurate cognitive map for men, the interleaved blocks reduced this difference for the first trials of the stationary blocks to an amount that rendered it non-significant. This effect of the non-stationary blocks could be explained by differences in strategy use. Women, relying mainly on navigational strategies based on egocentric representations, are less susceptible to the change of the environments. Men, more effective in the construction and use of allocentric representations and therefore performing generally better, are affected stronger by the interleaved blocks. Our results indicate that the male advantage in tasks of spatial navigation may rather be dependent on the experimental conditions, than of general nature. Further experimenting with interleaved non-stationary platform blocks, manipulating different types of cues (geometric or distal) will be helpful in delineating the contribution of strategy and cue use to the observed effect.

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Part IV

Ethics in Neuroscience

Ethics in the project

Background

We recognize the importance of work in the intersection of ethics and neuroscience. Ethics and neuroscience interact with each other: Neuroscientific knowledge has theoretical implications for fundamental anthropological and ethical concepts, and ethical criteria have practical implications for neuroscientific undertakings (ethics of neuroscience). When we come nearer to an understanding of the neural basis of our thinking and behaviour, we also have to consider the implications for science as well as for society in general. For such an enterprise we claim the need for expertise not only in the neurosciences, but also in policy, sociology, ethics, and the law to discuss the recent advances in the neurosciences. The field emerging from such fruitful discussion is termed “neuroethics”. Neuroethics is a new field concerned with the benefits and dangers of modern research on the brain, and furthermore with the social, legal and ethical implications of treating or manipulating the mind. We need to think about the morality and the ethics of what breakthroughs within the treatment or cure of brain diseases or disabilities will make it possible to do.

Evidently, neuroethics will overlap substantially with traditional issues in biomedical ethics, but goes beyond the topics of those as it begs distinctive questions for our intellectual and social thinking. This is because of the intimate connection between our brains and our behaviours, and from that on the special relationship between our brains and our selves, which has unique and dramatic implications for our perspective on us as persons, on ethics and from that on on social justice.

Doing patient-studies always requires thinking about the costs and benefits of the research project– this is especially important for studies where there is no direct, immediate benefit for the subjects. One has to care for responsible experimental design also because of this thought: There must be very good reasons to do this particular kind of study with these particular means – i.e. the results must be supposed to shed new light on interesting open questions in science which justify the effort the patients have to give. Even when the question of justification is quite difficult to answer, it is in the responsibility of the scientist to lay the fewest burden as possible on the patient and in the hand of the ethic committee to judge the study.

Within our project, thinking about the contact with patients was an important topic, as most of the team-members never have had experience with psychological studies, and especially not with patient-studies, before. This is why we had a special meeting with Prof. Prof. Dr. Albert to clarify questions on how to behave in the contact with patients. He recommended to imagine that the patients we want to investigate had severe brain surgery and often have psychological problems as well as physical deficits besides the ones we are interested in. That means that we should be aware that the patients might have speech or language problems or motoric deficits and also that they might react in unusual ways. Both sides made sure that there will always be an employee from the hospital around in case we would need someone.

Within discussions with the neurosurgeon we came to thoughts about questions like: What is under surgery there? The organ - of course, but does that imply that there happens a manipulation of the self? How does it feel to work in that area and to do surgery in the most sensitive organ?

An organ we only knew from papers and books? A major and long-lasting experience was the visit at the hospital. Most of the students got the chance, in groups of 2 or 3, to attend a brain-surgery. This was an outstanding experience!

History

Hippocrates' Oath is the basis today's medical ethics have evolved from. Taking Hippocrates' ideals from 500BC, the Hippocratic Oath has formed the basis of more recent medical oaths taken by students as they begin the practice of medicine. The chief tenants of this Oath are: "honour instructors in the medical arts", "practice for the benefit of patients; "do no harm"", "give no deadly medicine or substance to produce abortion", "abstain from mischief and corruption" and "care for a doctor-patient confidentiality".

From this on, standards of professional medical behaviour in research as well as in treatment were codified in the late 17th century. The AMA code of ethics was the first code to be adopted by a national professional organization. Those standards were officially adopted by medical associations in the mid-19th century. The current AMA code of ethics (2001) has additions to the previous one stressing the responsibility the doctor has towards the patient and the support of universal access to medical care.

After abuses of these standards within World War II, there was the need for a new codification: The Nuremberg Code (1947) is a set of 10 principles outlining the ethics of medical

research and ensuring the rights of human subjects. These principles include the need for informed, voluntary consent, the need that research must be based on animal studies or other rational justification. They ensure the avoidance and protection from injury, and unnecessary physical and mental suffering and the thought that risks to the subject shall not be greater than the humanitarian importance of the problem. Investigators must be scientifically qualified and the subject may terminate the experiment at any time.

Taking this as a basis, in the declaration of Geneva (1948) another oath was developed by the World Medical Association with the following main features the medical person has to follow: Recognize that one is in service to humanity, work in conscience and dignity in the practice of the art, give dutiful attention to the health of the patient, to colleagues and to traditions of the art, practice in accordance with the laws of humanity, respect for human life from conception and follow the principle that the duty takes precedence over racial, religious, political or social prejudices. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration".

The Declaration of Helsinki states that it is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The latest revision of the declaration (2000) states that "the well-being of the human subject should take precedence over the interest of science and society." Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject.

We can see that the declarations coevolve with the issues physicians and patients are confronted with. After World War II, for example, the inhuman experiments by physicians, made in the name of scientific progress, required an explicit statement that the principles of humanity should be of highest priority for any scientific enterprise. In the Helsinki Declaration, the more subtle dangers of volunteer participation in biomedical research had to be faced. This is what the ethics-commission took as a guideline in judging our particular study. We will now see how these abstract principles come into play in our actual work, in the way we choose the patients, how we work with them

Practical Implications

Choice of Patients

Together with Prof. Dr. Albert we discussed which patients we can include in our study and why we have to exclude some other patients. We took our time to investigate how to proceed best to inform patients. Also, we aimed to make sure that we only include those patients who will really help to investigate our paradigm such that we won't disturb those patients' lives who can't contribute to the study anyway. As it lies in his responsibility to ensure we only get access to patients we cannot harm and who will provide useful data, Prof. Dr. Albert set the following criteria:

- Epileptic patients are excluded from our study.
- Patients with severe psychological or physical problems are excluded, too.
- The lesions must be clear-cut such that we can rely on the results to be caused by what we think caused them.
- For the same reason, patients with additional diseases need to be excluded.

Information for Patients

To provide the patients with the most important information about our project, we prepared a brochure. It includes a short characterization of our team and our motivation within this study-project, as well as a description of the study and the offer to ask Prof. Dr. Albert in case of interest.

We formulated the informed consent forms in accordance with the revised Declaration of Helsinki. We had our own forms in addition to the hospital's general forms. With the signature on the form, the patient explains that he/she was informed satisfyingly on purpose and procedure of the study, had the possibility to ask questions and time to think thoroughly about the participation. Furthermore, he/she explains that there is an understanding that the participation is voluntary and can be terminated at any time without any negative consequences. Finally, it is stated that data will be handled anonymously.

Ethical Review

Another step, – much more complicated, as it showed up to be – was the procedure to get the admission to do the study by an ethical commission. We decided that we need the admission by

the ethics committee of the Ärztekammer Hannover. Prof. Dr. Albert as a medical doctor is obliged to ask the official instance which is in our case the Ärztekammer of the “Land”. Only later on, we would recognize that there is an ethics commission at the University of Osnabrück authorized to judge patient studies. Until then, we had to go through the application process required by the Ärztekammer Hannover.

At first, we found out how to construct such an application – and then wrote our proposal. After having discussed our proposal with Prof. Dr. Albert, we sent it to the Ärztekammer and got a short a feedback, saying that we have to rewrite it slightly in forms of their special requirements. We received a general form and a checklist about how this particular institution asks for applications. Thus, we changed our proposal and gave it another structure. Interestingly, we had to follow the standards for biomedical research and thus think about phases (like the phases in the development of a new medicine), and deny the usage of any medicine, x-raying etc.

Being satisfied with our proposal and having Prof. Dr. Albert’s approval, we now applied for the admission of our study. This was on 16.04.04. On 30.04.04 we got the answer from the committee with the comment that Prof. Dr. Albert must be the official and responsible head of the study, instead of Dr. Jacqueline Griego, as he is the medical instructor. Further, we received the invitation for the meeting of the commission for the judgement of medical research with humans where there will be the discussion of our proposal and an advice. Prof. Dr. Albert’s presence was required for this meeting. As this was a chance to see how ethics-commissions work and also to support Prof. Dr. Albert with detailed knowledge of our study, the motivation and the computer programs, two students - Saskia Nagel and Christian Mühl - accompanied him to Hannover at 24.05.04. At the meeting, there were the members of the commission: a lawyer, a medical ethicist, a pharmacologist, a microbiologist, a medical doctor and the manager. They had worked through our proposal and underlined again that Prof. Dr. Albert is the official leader of the study and thus the prior responsible for what we as a study project are doing. The Ärztekammer thus mainly advised him as the medical head what he has to care for in the setting of the “Berufsordnung”. In addition they state that what we are doing in fact is “biomedical research”, what was surprising for us but approved by the lawyer.

Concerning the content of our proposal, the commission mainly criticized that it lacks detailed inclusion and exclusion criteria. We tried to make clear that we will exclude patients whose physical and psychological state does not allow the participation and especially who show the

possibility of epilepsy. We will include patients with the kind of lesions and deficits fitting to our paradigms. It became clear that this needs to be described in more detail. This is in the responsibility of Prof. Dr. Albert who agreed to add the necessary information. Secondly, we were advised to improve the patient information with regards to the goal of the study. Unfortunately, this is problematic as we need naïve subjects at least in the affective priming task. But of course we will change that passage as good as possible.

Furthermore, they criticized that they cannot find out the real goal of the study and said that there should be less scientific background. Interestingly, in our case, exactly the scientific background and the further exploration of our hypotheses IS the goal of our study. It seemed to be uncommon for the committee to judge such kind of mere research proposals. Our study is completely unproblematic concerning the health of the patient, but also we do not help them directly with our experiments and the results of our study. There is no individual benefit for the participant, so it is very important that we really can make a scientific statement with the data we gain. We agreed to add the necessary information and also add a flow chart on our study project. When having done that we will again send the proposal to the commission and then they will decide whether to give us the admission.

On 01.06.04 we got a letter which shocked all of us: Besides the protocol stating what was discussed and advised at the meeting, there was a calculation with an account of 1.140 Euro.

Naturally, nobody was willing to pay that and thus Saskia Nagel went to see the legal adviser of the university, Andreas Osterfeld, to ask for help. They met several times to discuss the problem and to find a way how to deal best with the situation. We wanted to find out whether the commission was allowed to charge us. What followed was a long e-mail and telephone communication about legal topics concerning the future procedure between the legal adviser and Saskia Nagel who in turn informed Prof. Dr. Albert. Finally, we decided to ask Prof. Dr. Albert to refuse to pay and to ask the Ärztekammer to send the account to the IKW. This would bring the study project in a position to react and to ask the legal adviser to hand in revision. The IKW as an institution under the university which is an official public authority cannot be charged for the services of the commission. We handed in the revision and asked to set out the account “Aussetzungsantrag”. After that the Ärztekammer informed us that the letter was just an “information”, which is wrong in the legal understanding, as it only can be understood as an

administrative act. To be secure, the legal adviser recommended Prof. Albert to also hand in revision and ask to set out the whole procedure.

As we found out that the university has its own ethics commission which can judge our study, we decided to hand in our proposal there as well on 21.06.04 – even though Prof. Dr. Albert still preferred the admission of the Ärztekammer at that point in time.

The meeting of the committee took place on 14.07.2004. It was a much more cooperative atmosphere and also more productive than the meeting with the Ärztekammer. There was a short presentation and discussion, questions on the procedure and the methodology as well as on the background – and then we got the consent from the committee to do our study.

The state now is that we can start with the patient studies – we already ran the student population.

However we have to go on to think about how to handle the problem with the Ärztekammer as they still did not answer whether our revision is accepted or not. After another meeting with Prof. Dr. Albert and again a discussion with the legal adviser, we have to consider to cancel our application to the Ärztekammer. We now already have the admission to do the study and we do not need the Ärztekammer's admission anymore. However, here we need to take care which strategy to take – as we do not want to have the Ärztekammer in a bad mood as long as the financial topic is not clear yet.

The crucial consequence is that we were not yet able – and not allowed – to do patient studies. We had no other chance than to wait until we get the admission. Meanwhile, we decided to reformulate our paradigms and hypotheses such that we can test them on healthy subjects, i.e. on a student population. In case of the affective priming paradigm, we investigate hemispheric differences. In case of the Virtual Morris Watermaze we follow the idea that there are performance differences between genders. Thus, we investigate gender differences within the spatial navigation task.

Treatment of Patients

An obvious place to put to work ethical considerations would have been in dealing with patients. Although the experiment itself is considered harmless, we have to be sure patients are not harmed by the circumstances of the actual procedure. Prof. Dr. Albert, in addition to pre-selecting potential subjects, set some additional constraints in order to ensure the patients' safety.

So we would only have tested patients within the last ten days of their stay, and our whole visit would never have lasted longer than thirty minutes. We also thought about more subtle dangers of hurting the patients, just by saying potentially wrong things. If they asked something like “You’re coming to examine my damaged brain, right?” – what should we answer? And how would we proceed if it became obvious a patient was not able to finish our experiments? For this case, we agreed to abort the experiment and pretend that everything was alright in order not to further unsettle the patient. Most of these issues probably cannot be solved theoretically, but need to be dealt with as they occur. However, we found it useful to discuss these possible cases in order to develop a sense for the delicacy of the situation. Of course, none of these things became practically relevant as we have not conducted any patient studies so far – still we hope that future experimenters might want to come back to our provisional considerations.

Conclusions

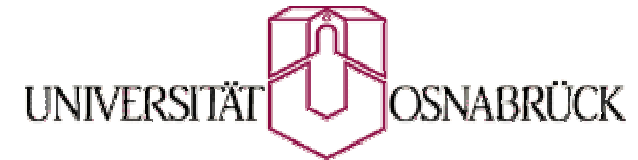
Within our project, we learned that ethics is not a purely theoretical subject. Not only did we have to deal with formal ethical requirements mentioned above when we designed the applications to the ethics committees, we also got to experience very concrete consequences for our project: For several month, we were not authorized to carry out our designed studies. However, one may wonder whether the delay really served the purpose to ensure ethical standards, or whether we were just caught in a trap of formal overkill. On the other hand, we do see the need for such formal frameworks and their strict application, as an argumentation along the lines of “obviously, nobody’s hurt” would have been nice for us personally, but of course shouldn’t be allowed in the general case. So it was interesting to see how the realization of the ethical standards we value so much in theory turned out to be a tedious obstacle in practice, partially because they were applied inappropriately concerning the biomedical research questions. This dilemma between idealist thinking and practical considerations, looking back, does in fact in itself constitute a valuable experience within the project.

Obviously, we are happy now that we finally received the admission from the commission to start the study. Formally, all of the students will finish the project in autumn 2004, but as we established the cooperation with the hospital and Prof. Dr. Albert in particular, we hope to finally do the study with patients and get the data we aimed for from the beginning of the project on.

Was ist Kognitionswissenschaft?

Vor wenigen Jahrhunderten begann man, Denken als 'mentale Berechnung' zu verstehen. Mit der Erfindung des Computers in diesem Jahrhundert konnte diese Idee modelliert werden. In den letzten Jahrzehnten haben Forscher verschiedener Disziplinen zusammengearbeitet, um mentale Prozesse und mentale Repräsentationen zu untersuchen und intelligente Systeme zu bauen. Daraus ist jetzt Kognitionswissenschaft entstanden, eine 'Interdisziplin' mit folgenden Schwerpunkten:

- die wissenschaftliche Erforschung von Geist und Gehirn,
- die Erklärung des menschlichen sprachlichen und nichtsprachlichen Verhaltens, und
- die Entwicklung künstlicher intelligenter Systeme.



MINI-Projekt

...wer ist dabei???



Wir möchten Sie einladen, am MINI-Projekt teilzunehmen!

Dabei handelt es sich um ein Forschungsprojekt der Universität Osnabrück in Kooperation mit der Paracelsus Klinik. Als Studenten des Fachbereichs Kognitionswissenschaft beschäftigen wir uns mit Fragen zu neuro-psychologischen Prozessen.



Zur Zeit untersuchen wir, wie Menschen visuelle Informationen verarbeiten.

Was tun Sie als Teilnehmer an unserem Projekt?

- Befindlichkeitsfragebogen ausfüllen
- Abbildungen auf Fotos bewerten

Wie lange dauert das ganze?

- das Experiment wird nicht mehr als 30 Minuten Ihrer Zeit beanspruchen
- die Aufgaben können Sie bequem in Ihrem Zimmer erfüllen

Bei Interesse oder weiteren Fragen wenden Sie sich bitte an Dr. Friedrich Albert (Leitender Arzt, Neurochirurgie).

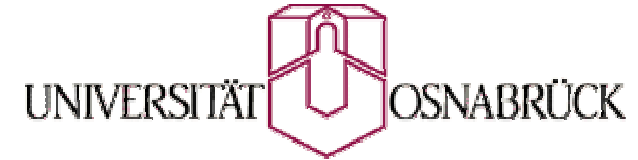


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MINI-Projekt

Mechanisms *In*
Neuropsychological Issues
...wer ist dabei???



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Zur Zeit untersuchen wir, wie Menschen visuelle Informationen verarbeiten.

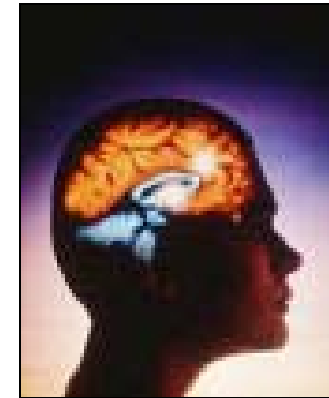
Was tun Sie als Teilnehmer an unserem Projekt?

- Sie beschäftigen sich zunächst mit einem Bilderrätsel
- Dann präsentieren wir Ihnen eine Landschaft aus einem Computerspiel, und Sie versuchen, sich darin zurechtzufinden.

Wie lange dauert das ganze?

- das Experiment wird nicht mehr als 30 Minuten Ihrer Zeit beanspruchen
- die Aufgaben können Sie bequem in Ihrem Zimmer erfüllen

Bei Interesse oder weiteren Fragen wenden Sie sich bitte an Dr. Friedrich Albert (Leitender Arzt, Neurochirurgie).



Wir freuen uns auf Sie!!!

Appendix B: Application for the ethics committee

Forschungsprojekt „Hemisphärenunterschiede bei Affektivem Priming“
Forschungsprojekt „Räumliche Navigation in einem Virtuellen Moris Wasserirrgarten“

A. Formales

1. Bezeichnung des Vorhabens
2. Ärztliche/r Leiterin/Leiter der klinischen Prüfung
 - 2.1 Name, Adresse
Prof. Dr. med. F. Albert
Neurochirurgie
Paracelsus Klinik
Am Natruper Holz 69
49076 Osnabrück
 - 2.2 Wissenschaftliches Curriculum vitae
(Erfahrungen mit klinischen Prüfungen)
3. Prüfstellen bzw. beteiligte Ärztinnen/Ärzte (siehe 2.)
4. Kostenträger

Entfällt, da es ein Studienprojekt des Internationalen Masterprogramms an der Universität Osnabrück (MINI: Mechanisms in Neuropsychological Issues) ist; deshalb entstehen keine Kosten.

5. Wurde schon ein Antrag gleichen Inhalts bei einer der in § 15 Abs. 1 der Berufordnung der Ärztekammer Niedersachsen angeführten Ethik-Kommissionen gestellt?

Nein, dies ist der erste Antrag mit diesem Inhalt.

B. Untersuchungsbeschreibung

1. Wissenschaftliche Beschreibung des Vorhabens

Der Zweck des “Mechanisms in Neuropsychological Issues” Studienprojekts ist es, praktische Erfahrungen mit der Entwicklung und Implementation von Paradigmen bezüglich kognitiver Funktionen zu erhalten, die bei Personen mit neurologischen Insults aufgrund von Tumor, Schlaganfall und anderer krankhafter Prozesse geschädigt sein können. In diesem Studienprojekt entwickeln wir zwei Forschungslinien. Die erste ist ein

innovatives Paradigma, um affektives Priming zu untersuchen. Hierbei geht es insbesondere um Personen mit Schädigungen in der rechten Hemisphäre und genereller um die Unterschiede, die bei solchem affektiven Priming zwischen linker und rechter Hemisphäre bestehen. Wir verwenden Bilder als Prime und als Zielreiz. Die Bilder werden entweder auf der rechten oder der linken Seite des visuellen Feldes präsentiert. Der zu untersuchende Effekt setzt an, kurz bevor die Information zu der anderen Hemisphäre ausstreut. Die zweite Linie der Studie umfasst den Einsatz eines virtuellen Morris Wasserirrgartens zur Untersuchung von Theorien zur räumlichen Navigation und Gedächtnisleistungen von Patienten mit Schädigungen im medialen Temporallappen. Außerdem entwickeln wir Perspektiven zu neuroethischen Fragestellungen und zur Theorie des Geistes, die in Beziehung zu unseren empirischen Untersuchungen stehen. Ziel des Studienprojektes ist es, praktische Erfahrungen zu sammeln, um die im Studium der Kognitionswissenschaft erworbenen Fertigkeiten zu integrieren: Wir nutzen die Kenntnisse aus der Informatik, um die Versuchsumgebung zu programmieren, und aus den Neurowissenschaften und Kognitionswissenschaften zur Implementation der Versuche und für die Entwicklung der Forschungsfragen aufgrund von Theorien im Bereich visuelle Kognition und räumliche Navigation.

Forschungsprojekt „Hemisphärenunterschiede bei Affektivem Priming“

Theorien über Hemisphärenunterschiede in der affektiven Verarbeitung

Hemisphärische Spezialisierung ist ein zentraler Bestandteil der Kognitionswissenschaft. In Hinblick auf die Verarbeitung von Stimuli mit affektivem Inhalt (wir benutzen die Achse *unangenehm-angenehm*), gibt es verschiedene Ergebnisse darüber, ob die Spezialisierung rechtshemisphärisch für jede Form von affektivem Inhalt ist, oder ob es eine weitere Spezialisierung von positiv-affektiv in der rechten Hemisphäre und negativ-affektiv in der linken Hemisphäre gibt (Klauer, 1998). Alternative Sichtweisen vermuten, dass die Spezialisierung rechtshemisphärisch negativ und linkshemisphärisch positiv ist, und schließlich, dass diese Effekte durch feine semantische Aufschlüsselung in der linken Hemisphäre und grobe semantische Aufschlüsselung in der rechten Hemisphäre zu erklären sind (z.B. Bolte, Goschke, & Kuhl, 2003). Unser Experiment ist nicht so entwickelt, dass sie alle diese theoretischen Blickpunkte einschätzen kann. Wir untersuchen nur, ob es einen Unterschied zwischen den Hemisphären in Bezug auf die Größe des Effekts (statistisch ausgewertet) gibt. Es geht uns hierbei um Patienten mit linken und rechten posterioren Kortexschäden. Wir wollen herausfinden, ob Patienten mit hemineglect empfänglich für Primingeffekte sind, die durch Stimuli im linken Gesichtsfeld ausgelöst werden, obwohl sie nicht berichten können, die Stimuli gesehen zu haben.

Unterschiede im zeitlichen Verlauf der Aufgaben zum affektiven Priming

Die Verarbeitung affektiv bewertbarer Inhalte von Stimuli ist aus evolutionären/entwicklungsgeschichtlichen Gründen bevorzugt. Positive Bewertung signalisiert eine sichere Umgebung und ist damit ein Hinweis, die Umgebung zu erforschen. Negative Bewertung induziert Vermeidungsstrategien (Davidson, 1999). Das heißt, dass es einen verlässlichen Primingeffekt in Hinsicht auf die Bewertung von Zielreizen gibt, die nach

angenehm/unangenehmen Primingreizen präsentiert werden (Fazio, 2001). Physiologisch erregende Stimuli (z.B. Bilder von Schlangen und Spinnen), die für 200 ms präsentiert werden, erzielen zuverlässige Primingeffekte, wenn ein Zielreiz bis zu 300ms nach der Präsentation des Primingreizes dargeboten wird (Lane, Reiman, Bradley, Lang, P.J., Ahern, Davidson, & Schwartz, 1997). Dieses automatisch aktivierte, affektive Bewertungspriming taucht nicht nach einer Zeitspanne länger als 300ms auf, nach der viele Effekte wie Wiederholungspriming, semantisches Priming, semantisches Inkongruenzpriming (Versace, Koenig, Royet, Bougeant, 2003), und Auswirkungen des Stimulusformats (Windmann, Daum, & Güntürkün, 2002) auftreten. Wir benutzen einen sehr kurz präsentierten Primingreiz und eine affektive Evaluationsaufgabe, weil der Effekt für kurze Zeitspannen auftritt und nicht durch weitere kognitive Verarbeitung beeinflusst wird. Also hat der Effekt eine relativ klare Interpretation und ist verlässlich (Fazio, 2001).

In der Aufgabe hat das Set von Primingreizen entweder positive (angenehme) affektive Valenz, negative affektive Valenz (unangenehm) oder neutrale Valenz. Diese Bewertung wurden in normierten Studien erhoben. Die Zielphotographien sind zu 90% neutral, zu 5% positiv und zu 5% negativ bewertet. Wenn die Zielreize alle die gleiche Valenz aufwiesen, könnten die Bewertungen der neutralen Photographien aufgrund des Antwort-Bias verfälscht werden. Jedoch werden die positiven und negativen Zielreize so angeordnet, dass diese Beeinflussung nicht entsteht. Wir erwarten, dass der Versuchsteilnehmer nach einem negativen Prime den neutralen Zielstimulus negativer bewertet im Vergleich zu der Bewertung desselben neutralen Stimulus nach der Darbietung eines positiven Primes. Entsprechend sollte ein positiver Prime eine positivere Bewertung des neutralen Zielreizes bewirken, als die nach einem negativen Prime.

Wir vermuten, dass die affektive Valenz des Primes die Bewertung jegliches Stimulus' beeinflusst. Interessant ist nun, ob es die Unterschiede in gleicher Qualität auch dann gibt, wenn wir die Antwort der rechten Hemisphäre mit der der linken Hemisphäre vergleichen.

Forschungsprojekt „Räumliche Navigation in einem Virtuellen Morris Wasserirrgarten“

Die Themen Placelearning und Navigation sind seit langer Zeit Untersuchungsgebiete im Bereich der Forschung, die sich mit der biologischen Basis von Lernen und Gedächtnis beschäftigt. Der Hippocampus, der eine wichtige Rolle für Gedächtnisbildung spielt, scheint außerdem die Basis für das Erstellen von 'Kognitiven Karten' zu sein (z.B. O'Keefe & Nadel, 1978). Zudem wird seine Notwendigkeit für die Assoziation von Umweltreizen mit bedeutungsvollen Mustern in Hinsicht auf Gedächtnis und Placelearning angenommen (z.B. Rudy & Sutherland, 1995). Große Teile der Forschung auf dem Gebiet Placelearning wurden mit Ratten und Mäusen im Morris Wasserirrgarten durchgeführt (Morris, 1981, Morris, 1997).

In der Aufgabe im Wasserirrgarten lernen die Tiere, eine im Wasser versteckte Flucht-Plattform zu lokalisieren. Normalerweise lernen Tiere, die Plattform zu finden, ohne äußere, lokale Hinweise zu haben (die Poolwand ist überall gleich aussehend und der Boden des Pools kann nicht gesehen werden). Das zeigt, dass Merkmale im Hintergrund (Dinge, die außerhalb des Pools sichtbar sind) für das Placelearning ausreichend sind. Tiere, die die Plattform lokalisiert haben, können diese wiederfinden, wenn sie aus dem Pool genommen und anschließend an anderer Stelle wieder in den Pool gesetzt werden. Es können sogar einzelne Merkmale im Hintergrund entfernt werden – solange

mindestens zwei Hinweise vorhanden sind, wird die versteckte Plattform gefunden. Diese Ergebnisse sind – neben Einzelzellableitung von „place cells“ im Hippocampus – die Basis für psychologische Theorien zum Placelearning. Man nimmt aufgrund dieser Ergebnisse an, dass der Hippocampus verantwortlich ist für das Erstellen einer kognitiven Karte während der Erkundung der Umgebung.

Bei Tieren hat man die Effekte von Läsionen, pharmazeutischen Manipulationen, genetischem Hintergrund, Altern, und pränataler Umwelt intensiv untersucht. Es ist allgemein anerkannt, dass Lernen durch Schäden am Hippocampus gestört wird, und dass die erstmalige Aneignung von Gedächtnisinhalten abhängig ist von hippocampaler synaptischer Plastizität (Morris, 1997).

Placelearning ist außerdem mit anderen Gehirnregionen verbunden – zu welchen genau und in welcher Weise ist zur Zeit stark debattiert (z.B. Sutherland, Kolb, Whishaw, 1982). Ein Setting, welches dem Morris Wasserirrgarten ähnelt, wird seit Kurzem in einer virtuellen Version für Menschen getestet.

Die virtuelle Umgebung ermöglicht eine bessere Kontrolle als in der realen Umgebung und außerdem sind Vergleiche zwischen den Tierexperimenten der letzten 20 Jahre mit der Aufgabelösung durch den Menschen bei einer ähnlichen Aufgabe möglich.

Obwohl es keine Hinweise auf propriozeptiver und vestibularer Ebene gibt, zeigen die existierenden Ergebnisse von Humanstudien, dass Menschen ähnlich wie Ratten aufgrund der Konfiguration von in Entfernung befindlichen Stimuli lernen (Hamilton, Driscoll, & Sutherland, 2002). Außerdem gibt es Hinweise darauf, dass das virtuelle *Placelearning* ähnliche neuronale Strukturen wie den Hippocampus und mit ihm in Beziehung stehende Strukturen beansprucht (Maguire, Burgess, O’Keefe, 1999).

Zum jetzigen Zeitpunkt der Entwicklung des virtuellen Wasserirrgartens sind wir hauptsächlich daran interessiert, inwiefern es Unterschiede gibt zwischen der Performance der Teilnehmer mit mediotemporalen Schädigungen und Gesunden sowie anderen Patientenpopulationen. Wir steuern also bei zu den wenigen Untersuchungen, die es mit Patientenpopulationen gibt. Dr. Griego war beteiligt an der frühen Entwicklung des virtuellen Morris Wasserirrgartens, welchen wir nutzen, und außerdem arbeitet sie mit dem Entwickler zusammen, Dr. Derek Hamilton am, Canadian Center for Behavioural Neuroscience’, um das Paradigma weiterzuentwickeln.

2. Vorlage des Prüfplans und der Dokumentationsbögen

Forschungsprojekt „Hemisphärenunterschiede bei Affektivem Priming“

Das Experiment beginnt mit dem Ausfüllen eines Befindlichkeitsfragebogens und dem Komplettieren einer Linien-Bisektionsaufgabe durch den Teilnehmer. Dann wird dem Teilnehmer am Computer erklärt, dass er im Folgenden Photographien bewerten wird. Die Bewertung reicht von –4 (sehr unangenehm) bis +4 (sehr angenehm). Der Teilnehmer wird darüber informiert, dass wir interessiert daran sind, inwiefern Ablenkung seine Bewertung beeinflusst. Die Anleitung beginnt mit dem Hinweis, dass es ein Fixationskreuz gibt, das fokussiert werden soll. Dann erscheinen einige kurz dargebotene Bilder auf dem Bildschirm – der Teilnehmer wird gebeten, weiterhin das Kreuz zu fixieren.

Die Teilnehmer können Ihr Kinn während der Aufgabe auf einer Kinnstütze betten, so dass Ihnen die Fixation leichter fällt. Dann werden sie Bilder in der Mitte des Bildschirms

sehen. Sie sollten nun so schnell wie möglich eine Bewertung auswählen – wir sind interessiert an ihrer *direkten* Reaktion auf die Bilder.

Es gibt 10 Probeläufe für die Bewertungsaufgabe. Nach den Probeläufen erscheint auf dem Bildschirm die Information, dass die Aufgabe nun beginnt.

Nach 500ms wird im rechten oder im linken Gesichtsfeld, 40° vom Zentrum entfernt, ein Primingbild präsentiert. Dieser Prime wird sehr kurz – für 200ms – dargeboten, verschwindet, und der Bildschirm bleibt für 50ms leer. Dann erscheint der Zielreiz in der Mitte (horizontal und vertikal) des Monitors. Unter dem Zielreiz befindet sich die Bewertungsskala, die aus 9 von –4 bis +4 gekennzeichneten Kreisen besteht. Die Bewertung wird durch einen Mausklick auf den entsprechenden Kreis vorgenommen – dann wird ein <abgeben> Feld mit der Maus angeklickt. Die Teilnehmer bewerten 90 Photographien. Die durchschnittliche Zeit der Bewertung eines Bildes dauert ca. 15 Sekunden; das heißt, dass die ganze Aufgabe erwartungsgemäß 21 Minuten dauern wird

Nach dem letzten Durchlauf erscheint ein Text auf dem Bildschirm, der den Teilnehmer informiert, dass das Experiment beendet ist und nun der Versuchsleiter erklären wird, was der Zweck der Untersuchung ist, wie die Forschungsfrage lautet und dass Fragen gestellt werden können. Die Untersuchung endet mit diesem Gespräch zwischen dem Teilnehmer und den die Untersuchung durchführenden Studenten.

Forschungsprojekt „Räumliche Navigation in einem Virtuellen Moris Wasserirrgarten“

Teilnehmer werden zunächst einen “transverse patterning task” ausführen. Dieser besteht aus einem Lernprozess, durch Versuch und Irrtum: Wenn ein Stimulus ‘A’ gepaart ist mit einem Stimulus ‘B’, dann ist die richtige Antwort Stimulus ‘A’, wenn Stimulus ‘B’ mit Stimulus ‘C’ gepaart ist, dann ist Stimulus ‘B’ die richtige Antwort, und wenn Stimulus ‘A’ mit Stimulus ‘C’ gepaart ist, dann ist Stimulus ‘C’ die korrekte Antwort. Die Durchläufe werden mit zufälliger Präsentation des Stimuluspaares wiederholt, bis es entweder 14 korrekte aufeinanderfolgende Antworten gab oder 100 Paare präsentiert wurden. Das dauert ca. 8 Minuten, wenn der Teilnehmer die Aufgabe nicht lernt und ca. 2 Minuten, wenn er sie lernt. Diese Aufgabe wird durchgeführt, weil gezeigt wurde, dass es Unterschiede in der räumlichen Navigation im Wasserirrgarten gibt zwischen Patienten, die die Aufgabe erfüllen können und denen, die es nicht können.

Die virtuelle Umgebung stellt einen kreisförmigen Pool in der Mitte eines quadratischen Raumes dar. Die Poolwände sind über die Wasseroberfläche verlängert. Das Wasser ist in einer undurchsichtigen blauen Farbe. Die Merkmale im Hintergrund sind Türen, Fenster und Bilder an der Wand.

Die Teilnehmer werden informiert, dass sie in „Erste Person Perspektive“ in eine virtuelle Umgebung platziert werden und dass sie über die Pfeiltasten auf der rechten Seite der Tastatur navigieren können: Der <aufwärts> Pfeil bewegt sie vorwärts, der <links> Pfeil bewegt sie nach links und der <rechts> Pfeil bewegt sie nach rechts. Die Teilnehmer werden informiert, dass sie in ein kreisförmiges Wasserbassin gelassen werden, aus dem man so schnell wie möglich auf eine Plattform entkommen soll. Sobald sie über die Plattform schwimmen, wird diese aus dem Wasser auftauchen und eine Botschaft auf dem

Bildschirm wird sie davon benachrichtigen, dass sie die Plattform gefunden haben. Wenn die Plattform innerhalb von 60 Sekunden nicht gefunden wird, wird diese aus dem Wasser gehoben und der Teilnehmer soll zu ihr schwimmen. Dort kann er eine Weile bleiben und sich umschaun, die Plattform allerdings nicht verlassen.

Danach beginnt ein neuer Versuch, der mit Blick auf die Poolwand startet. Das Ganze wird 4 Mal wiederholt. Nachdem vier Durchläufe beendet wurden, wird den Teilnehmern mitgeteilt, dass die Plattform verschoben wurde und ein neuer Test mit der Suche nach der Plattform startet.

Es wird Durchläufe von jeweils 4 Versuchen geben – diese werden insgesamt höchstens 24 Minuten dauern, da es die Begrenzung auf 60 Sekunden gibt um die Plattform zu finden.

Nach Beendigung der Aufgabe erscheint auf dem Bildschirm der Dank an die Teilnehmer für Ihre Mitarbeit. Die Untersuchung endet mit einem Gespräch zwischen Teilnehmer und den die Untersuchung durchführenden Studenten über das Experiment und den relevanten Forschungshintergrund.

Anschließend wird die Performance berechnet aus der gesamten Schwimmzeit, der Länge des Schwimmweges und der Menge der Zeit, die im richtigen Quadranten des Pools verbracht wurde.

3. Vorgesehene Gesamtdauer und Beginn des Vorhabens

Alle Vorbereitungen sind bereits getroffen. Sobald eine Bewilligung der Ethikkommission vorliegt, kann mit den kognitiven Studien begonnen werden.

4. Probandenauswahl

(z. B. Ein- und Ausschlußkriterien, Anzahl der Probanden)

Aufgrund der Forschungsfrage werden Patienten ausgewählt, die eine Hirnverletzung haben (posterior links/rechts, mediotemporale Schädigungen). Für die operative Kontrollgruppe werden Patienten, die sich einer Operation im Bereich der Wirbelsäule unterziehen mussten, ausgewählt.

Pro Gruppe sollten 15 Probanden befragt werden.

Die Teilnehmer an dem Experiment werden von Prof. Dr. Albert gefragt, ob sie an der Studie teilnehmen möchten. Sie erhalten zusätzlich Informationen, die von den Projektteilnehmern vorbereitet wurden und eine Broschüre. – Es werden nur solche Patienten ausgewählt, deren physische und psychische Verfassung die Teilnahme an der Untersuchung grundsätzlich zulässt und deren Krankheits- bzw. Behandlungsverlauf hierdurch nicht belastet wird.

Die erforderlichen Einwilligungsbestätigungen werden durch die Klinik eingeholt. Die kognitiven Aufgaben wurden nach Absprache mit Prof. Albert so entwickelt, dass die Durchführung nur 30 Minuten dauert. Die Untersuchung findet in den Räumen der Patienten oder in einem Konsultationszimmer statt – je nachdem, wie der Patient es wünscht.

5. Art der Prüfung (bei Arzneimittel: Phase)

5.1. diagnostische Prüfung?

Nein, entfällt.

5.2. therapeutische Prüfung?

Nein, entfällt.

5.3. Verträglichkeitsprüfung?

Nein, entfällt.

5.4. epidemiologische Prüfung?

Nein, entfällt.

5.5. sonstige Prüfung?

Kognitives Problemlösen

6. Finden folgende Bestimmungen Anwendung:

6.1. Arzneimittelgesetz?

Nein, entfällt.

6.2. Medizinproduktegesetz?

Nein, entfällt.

6.3. Strahlenschutzverordnung?

Nein, entfällt.

6.4. Röntgenverordnung?

Nein, entfällt.

6.5. EN 540, Klinische Prüfung von Medizinprodukten?

Nein, entfällt.

6.6. Grundsätze für die ordnungsgemäße Durchführung der klinischen Prüfung von Arzneimitteln?

Nein, entfällt.

6.7. Revidierte Deklaration von Helsinki des Weltärztebundes?

Ja, findet Anwendung.

Alle Stimuli wurden vor der Verwendung im Experiment begutachtet – und obwohl nicht alle Bilder in der Affektiven Priming Aufgabe angenehm sind, so sind sie doch von ähnlicher affektiver Valenz wie Bilder, die man im Fernsehen oder in der Zeitung sieht. Sämtliche Daten werden streng vertraulich behandelt und die Namen der Teilnehmer werden weder in der Analyse noch im Bericht erwähnt. Jegliche Listen von Teilnehmernamen und Identifikationsnummern, die für die Vereinfachung der Datensammlung benötigt werden, werden separat von der Versuchsumgebung in einem verschlossenen Raum verwahrt. Den Teilnehmern wird während der Information über den Versuchsablauf erklärt, dass sie jederzeit und aus jedem Grund die Teilnahme beenden können. Alle Stimuli sind auf Anfrage verfügbar, sollten Fragen bezüglich des Inhalts auftreten. Die Teilnehmer werden am Ende über das Ergebnis des Versuchs informiert. Die Studenten, die die Experimente durchführen, werden allen erforderlichen Klinikweisungen folgen. Die kognitiven Aufgaben werden in einem Konsultationsraum oder bei Wunsch der Patienten auch im Krankenzimmer gestellt. Das Klinikpersonal ist in der Nähe, so dass im Bedarfsfall jederzeit sachkundige Betreuung gewährleistet ist. Patienten, die eine Tendenz zu epileptischen Anfällen aufweisen, kommen als Teilnehmer nicht in Frage.

6.8. § 15 der Berufsordnung der Ärztekammer Niedersachsens?

Da keine biomedizinische oder epidemiologische Forschung betrieben wird, kommt der § 15 der Berufsordnung der Ärztekammer Niedersachsens nicht zur Anwendung.

7. Welche Vorprüfungen sind durchgeführt worden?

Entfällt eigentlich; dennoch haben sich Studenten zu Testzwecken der Prozedur unterzogen.

8. (Bei Arzneimittelprüfungen) - entfällt -
Ergebnisse der pharmakologisch-toxischen Prüfung

8.1. Entfällt die pharmakologisch-toxikologische Prüfung nach § 42 Satz 2 Arzneimittelgesetz?
(wenn ja, Begründung)

8.2. (wenn nein) Wurden die Ergebnisse bereits geprüft?

8.2.1. (wenn ja) Benennung der überprüfenden Stelle

8.2.2. (wenn nein) Vorlage der Ergebnisse

8.3. Wortlaut der Mitteilung des für die pharmakologisch-toxikologische Prüfung verantwortlichen Wissenschaftlers an den Leiter der klinischen Prüfung über die Ergebnisse der pharmakologischen-toxikologischen Prüfung und die voraussichtlich mit der klinischen Prüfung verbundenen Risiken gemäß § 40 Abs. 1 Satz 1 Nr. 7 Arzneimittelgesetz.

9. (Bei Medizinprodukteprüfungen:) - entfällt -
Ergebnisse der Laborprüfungen, ggf. Ergebnisse der Prüfungen zur biologischen Sicherheit, ggf. Ergebnisse der Tierversuche

Bei Produkten, deren Risiken die Ethikkommission nicht überblicken kann, kann ggf. eine Bescheinigung des Sachverständigen oder einer benannten Stelle verlangt werden, dass das Produkt – bis auf die klinischen Daten – die grundlegenden Anforderungen der dafür geltenden EG-Richtlinie erfüllt.

10. Mögliche Komplikationen und/oder Risiken

Es gibt keine dokumentierten Risiken für Operationspatienten bei der Bearbeitung kognitiver Probleme. Da es sich um eine fast „alltägliche“ Situation handelt, vergleichbar mit Fernsehen, werden keine außergewöhnlichen oder risikoreichen Situationen erwartet.

11. Risiko-Nutzen-Abwägung

Aufgrund des geringen Risikos, ist der theoretische Nutzen der Daten für Forschungszwecke bzgl. Affektives Priming und räumlicher Kognition sehr hoch.

12. Zwischenauswertung und Abbruchkriterien

Zwischenauswertungen sind nicht geplant. Abbruchkriterien gibt es nur auf der persönlichen Ebene, d.h., es ist dem Probanden selbstverständlich erlaubt, den Test jeder Zeit abubrechen.

13. Wie und in welcher Höhe finden Zahlungen an die Teilnehmer der Studie statt?

Es handelt sich in diesen Forschungsprojekten ausschließlich um Freiwillige. Zahlungen finden nicht statt.

14. Form und Inhalt der Probandeninformation) **bitte in**

-siehe Anlage-

15. Einwilligungserklärung

) **Kopie**

- siehe Anlage-

16. Versicherungsbestätigung

) **beifügen**

(gesetzlich vorgeschrieben nur bei der klinischen Prüfung von Arzneimitteln und Medizinprodukten)

- entfällt -

Anlage: *Einwilligungserklärung und Probandeninformation*

Appendix C: Informed consent forms

Forschungsprojekt „Hemisphärenunterschiede bei Affektivem Priming“

Einwilligungserklärung für die Teilnahme an einer Studie
Fotografie Bewertungsaufgabe

Die Sitzung fängt mit dem Ausfüllen eines kurzen Fragebogens über die Gemütsverfassung an, danach soll eine kurze Aufgabe erfüllt werden, bei der eine Linie durch die Mitte einiger Figuren gezeichnet werden soll, die auf einem Blatt Papier gedruckt sind. Dann werden Sie an einem Computerbildschirm Fotografien sehen und sollen einstufen, wie angenehm Sie diese empfinden. Wir sind daran interessiert, wie sich Ihre Bewertungen durch Ablenkung verändern.

Deswegen werden einige andere Fotografien kurz aufgezeigt, bevor Sie die zu bewertende Fotografie sehen. Wir bitten darum, dass Sie so schnell wie möglich die Fotografie bewerten, denn wir sind an der unmittelbaren Reaktion auf die Fotografie interessiert. Die Anweisungen für die Aufgaben erscheinen auf dem Computerbildschirm und werden auch von dem Sitzungsleiter gegeben. Es steht Ihnen jederzeit frei, die Aufgabe zu beenden. Insgesamt sollen 90 Fotografien bewertet werden.

Die Sitzung findet in Ihrem Zimmer oder in einem nahegelegenen Besprechungszimmer statt. Beide Räumlichkeiten befinden sich in der Nähe von Klinikpersonal, für den Fall, dass Sie dies benötigen sollten oder ein Notfall eintritt.

Nachdem die Aufgabe erfüllt wurde, wird der Experimentleiter den Zusammenhang dieser Aufgabe und unserer Forschung erklären. Wenn Sie wollen, dürfen Sie Fragen stellen. Die Sitzung wird ungefähr 30 Minuten dauern.

Nicht alle Fotografien sind angenehm, aber auch nicht unangenehmer als Bilder, wie sie im Fernsehen oder in der Zeitung zu sehen sind. All Ihre Daten werden streng vertraulich behandelt und der Name des Teilnehmers wird nicht bei der Analyse oder in Berichten verwendet. Listen mit Patientennamen, Identifikationsnummern und medizinische Informationen, die für die Erleichterung der Datenerfassung geführt werden, werden getrennt von den experimentellen Bereichen in einem verschlossenen Raum aufbewahrt. Wenn Sie an den Resultaten der Studie interessiert sind, können Sie Ihre Kontaktinformationen an den Sitzungsleiter geben, damit Sie zukünftig informiert werden können.

Ich erkläre, dass ich damit einverstanden bin, an dieser Studie freiwillig teilzunehmen. Ich habe obige Informationen gelesen und meine Rechte zur Einhaltung der Diskretion bezüglich jeder medizinischen Information und jeder Antwort, die während der Sitzung von mir gegeben wurde, verstanden und dass ich dabei keines meiner Rechte als Patient aufbebe.

Teilnehmer Unterschrift

Datum

Teilnehmer Name (Druckschrift)

Experimentleiter Unterschrift

Datum

Forschungsprojekt „Räumliche Navigation in einem Virtuellen Morris Wasserirrgarten“

Einwilligungserklärung für die Teilnahme an einer Studie
Virtuelles Wasserbecken Navigationsaufgabe

Sie führen zuerst eine kurze Aufgabe mit Mustern durch. Das heißt, dass durch Ausprobieren gelernt werden soll, welche Figuren zusammengehören.

Danach kommt die Hauptaufgabe die darin besteht, dass Sie einen Weg durch ein spielerisches Wasserlabyrinth finden.

In dieser virtuellen Umgebung werden Sie sich in einem kreisförmigen Wasserbecken sein, der sich in der Mitte eines quadratischen Raumes befindet. Sie werden das Wasserbecken aus Ihrer Perspektive sehen. Sie können so tun, als würden Sie in diesem Wasserbecken schwimmen, indem Sie die Pfeiltasten auf der rechten Seite der Tastatur drücken.

Sie werden in dieses kreisförmige Wasserbecken gesetzt und sollen daraus wieder fliehen, indem Sie so schnell wie möglich auf eine Plattform klettern. Wenn Sie über eine solche Plattform schwimmen, wird sich diese aus dem Wasser erheben und eine Nachricht wird auf dem Bildschirm angezeigt, dass Sie die Plattform gefunden habe. Sie werden ein paarmal nach dieser Plattform suchen.

Die Sitzung findet in Ihrem Zimmer oder in einem nahegelegenen Besprechungszimmer statt. Beide Räumlichkeiten befinden sich in der Nähe von Klinikpersonal, für den Fall, dass Sie dies benötigen sollten oder ein Notfall eintritt.

Nachdem die Aufgabe erfüllt wurde, wird der Experimentleiter den Zusammenhang dieser Aufgabe und unserer Forschung erklären. Wenn Sie wollen, dürfen Sie Fragen stellen. Die Sitzung wird ungefähr 30 Minuten dauern.

Nicht alle Fotografien sind angenehm, aber auch nicht unangenehmer als Bilder, wie sie im Fernsehen oder in der Zeitung zu sehen sind. All Ihre Daten werden streng vertraulich behandelt und der Name des Teilnehmers wird nicht bei der Analyse oder in Berichten verwendet. Listen mit Patientennamen, Identifikationsnummern und medizinische Informationen, die für die Erleichterung der Datenerfassung geführt werden, werden getrennt von den experimentellen Bereichen in einem verschlossenen Raum aufbewahrt. Wenn Sie an den Resultaten der Studie interessiert sind, können Sie Ihre Kontaktinformationen an den Sitzungsleiter geben, damit Sie zukünftig informiert werden können.

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Teilnehmer Unterschrift

Datum

Teilnehmer Name (Druckschrift)

Experimentleiter Unterschrift

Datum

A framework to systematize positions in Neuroethics

Saskia Nagel & Nicolas Neubauer

Abstract

Progress in Neuroscience advances rapidly and promises to change some of the basic concepts we have about ourselves. The field of Neuroethics is concerned with the resulting ethical implications. In this paper, we propose a framework to systematize the questions and positions in this context. We start with the discussion of three concrete cases around the topics of treatment/enhancement, personhood and privacy. For each case, we get a set of axes along which standpoints may vary. Finally, we generalize the particular axes of each case and arrive at a three-dimensional coordinate system spanned by the axes of “Liberty of Denial”, “Liberty of Use” and “Scepticism”. With this, we hope to provide a common language simplifying interdisciplinary dialogue and communication with the public.

Introduction

Motivation

During the last few decades, progress in neuroscience has advanced rapidly: Imaging techniques have been improved in terms of temporal as well as spatial resolution, providing us with ever increasing amounts of data about the brain. Sophisticated analysis tools have achieved big successes in turning these data into valuable information, and work in modelling has led to the creation of theories linking this information back to actual brain processes. Finally, we are entering an age where even manipulation of the brain on physical, chemical and physiological levels becomes possible.

This kind of progress might change the way we look at the world and ourselves like only a few developments before in the history of science: The so called Copernican Shift more than 300 years ago led to modern science as it showed that the

earth is not central to the astronomical system. Later, Darwin and even later Freud led to similar profound revolutions concerning our ideas about the nature of mankind. Today’s neuroscience promises to reveal insights that may force us to rethink fundamental concepts about what is special about us, some of which have been around for thousands of years.

How do we deal with these changes? How does our idea of man change? How do we want to define the borders between desirable technical progress and uncontrollable inhuman developments? How do we set criteria about what is normal and what is not in lights of new accomplishments in psychopharmacology and psychosurgery?

Shortly, how can we distinguish between good and bad when confronted with many qualitatively new options? Traditionally, this distinction is the domain of ethics, providing guidelines to derive judgements on concrete issues based on abstract principles. In this paper, we will investigate the role of ethics in the field of neuroscience.

Definition

Progress in medicine and life sciences has already lead to the formation of ethical frameworks for questions arising around human life, identity and dignity. One might think that these frameworks can also be applied, perhaps modified, to questions arising in neuroscience.

Medical ethics provides the foundations to define professional medical behaviour in research as well as in treatment. This involves issues like self-determination of the patient, doctor-patient confidentiality, and the huge field of death: When is it safe to be declared, when is it appropriate to be facilitated? Based on the Hippocratic Oath 2500 years ago, the principles of medical ethics have been codified in a number of declarations evolving to incorporate newest medical achievements and changes in moral standards. Central to all these

declarations is the idea that the benefit of the patient should be of highest priority for physicians, ranking higher than, for example, benefits for science or society. In the late 17th century, the AMA code was the first code to be adopted by a professional organization. 1948, the declaration of Geneva re-established values violated in World War II. Recently, the latest revisions of the declaration of Helsinki include emerging issues in biomedical research.

Bioethics has become a new field on its own to deal with these issues. Triggered by latest insights and inventions, questions about organ transplants, embryonic research or genetics have arisen. This is heavily related to medical ethics as the same fundamental considerations about benefit and service to humanity are at stake. But at the same time, the scope of bioethics exceeds the scope of medical ethics. Non-human life needs to be taken into consideration as, for example, we achieve means to modify existing species. Hence, bioethics today seems to have absorbed medical ethics.

Neuroethics is a field first mentioned about a decade ago, intended to investigate topics that are created by new technological insights and which are not yet covered by existing ethical frameworks, much like bioethics earlier. The specific ethics of neuro- and brain sciences treats the implications of discovering the secrets of the organ which is responsible for intelligence, conscience and individuality. Where bioethics redefines life, neuroethics is now in the need to redefine mind. Questions of personality, (self-) consciousness or emotions must be investigated on the basis of recent experimental results.

Although neuroethics is clearly related to medical ethics and bioethics, we cannot expect those to concretely answer questions arising from neuroscience, as we have shown some of these questions to exceed the scope of these disciplines. It seems that neuroethics will need to become a subdiscipline within the framework of bioethics, depending on common principles, but constructing its own particular domain.

In 2002, the first world conference on neuroethics, “Neuroethics – Mapping the Field” took place, bringing together neuroscientists, philosophers, lawyers, and public policy makers. The participants realized the challenge lying ahead of them and started laying out the scope and borders of the new-to-be-founded discipline.

Beyond discussing actual scientific contents, sensitizing the scientific community and the general public turned out to be an important task for the future.

Procedure

In this paper, we want to examine a few critical cases and demonstrate the need for ethical guidelines. We will not provide definite answers, but try to show the axes along which possible positions might vary. We will see whether some of these axes will show up in several different cases and could thus be generalized to basic dimensions in the mapping process. By this, we hope to develop a framework suitable for systematic description and analysis.

First, three case studies in the central topics of treatment vs. enhancement, personality and privacy will be introduced and discussed. For each case, the particular ethical questions will be worked out. Potential solutions will be proposed, and the underlying positions will be identified, which we will then try to conceptualize as points in a space spanned by the axes we are looking for.

After discussing the individual cases, an attempt will be made to unify the positions and axes we derive. This should provide a coordinate system which makes it possible to position standpoints relative to others in a generalizable way going beyond single, concrete examples. Like this, clusters of individual opinions may be found, simplifying the identification of “camps” within the field of neuroethics. Furthermore, knowing one’s own position and the position of a set of possible choices would ideally, by finding the closest alternative, make it easier to derive decisions consistent with one’s convictions.

Case Studies

Why cases?

We now present three cases, roughly in order of their expected occurrence. Concrete cases help us make intuitions explicit and better see which problems may arise – cases put some flesh to the bones of our abstract concerns. At first, we will take a closer look at the treatment/enhancement

distinction which already plays a role in every-day situations today. Secondly, we go into the nearer future when investigating how topics like informed consent can be handled in psychosurgery, raising questions of personality and personhood. Finally, we will see that with the emergence of brain-imaging methods, applications in “brain reading” may not be too far away – we will investigate the privacy issues involved. For each case, we will at the end present axes which enable us to locate different positions in the space of possible opinions.

Treatment/Enhancement

The growing ability to manipulate brain function can be used to treat dysfunctions of the brain in case of (mental) illnesses as well as to enhance the brain processes of healthy individuals. As far as we can see now, there is no clear-cut boundary between treatment and enhancement, but rather we see a complex continuum with many nuances in the field of medical services (from uses which are completely detached from health-care to uses in life-threatening situations). We can achieve specific mental and behavioural changes by using neurochemicals. Drugs which are approved for and mainly used to treat neurological and psychiatric diseases lately are used more and more to enhance healthy people’s capacities.

One example becoming increasingly important, especially in US schools and colleges, is the usage of psychopharmacology against attention-deficit/hyperactivity disorder (ADHD). Treatment with methylphenidate as psychopharmacological interventions is used as a study aid as it helps focussing on topics by increasing the activity of dopamine. Stimulants are used by many more people than there are people having the disorder for which it was developed. ADHD is found only in about 4-5 percent of children, but about 16% get the prescription.

There are two different dilemmas here: First, how much do we want to allow such manipulations? Should we reserve it for extreme cases, or maybe not use it at all? Or shouldn’t we rather go and enjoy the benefits of modern technology? Second, what about pressures concerning such interventions? Should they remain voluntary, is that possible at all? Or are

there cases where people should be forced to use drugs?

Reality has shown that if there is a drug which makes us perform better, feel better, we will want to take it – it just looks better for us to have it than not to have it. On the other hand, extending our capabilities beyond the norm seems unnatural, and dangerous both concretely (e.g., unpredictable long term effects) and in more abstract ways (e.g. concerning our idea of man).

These standpoints above hint at the two ends of a continuum of opinions regarding this dilemma. Adopting one of them would lead to either a completely restrictive position rejecting any use of psychopharmacological means, or to an extremely liberal one, embracing all possible uses. In practice, most questions are located in the area between these two extremes. Some cases are commonly accepted to be justified occasions for psychopharmacological treatment (like Alzheimer’s Disease or heavy psychoses and neuroses), just as there are other cases which a majority would judge illegitimate (doping children for better performance at school). The actual controversies emerge in border cases where clear-cut judgements are no longer possible. Although we, in the beginning, had a strong intuition that the giving of Ritalin to healthy children, for example, would be an instance of clearly illegitimate uses, it turns out that a more liberal view on this topic might also be theoretically justified.

A central point in this concrete case and other related discussions is the notion of “normality”. Restoring or establishing normality (“treatment”) would be considered legitimate by many positions; the differences between these positions then stem from their different definitions of normality. If we consider the norm the to be way we are and whatever happens to us, there is no way in which medical procedures could move us towards normality. We might say normal is how we are in the absence of dramatic external influences; then restoring a person’s mental state after a traumatic experience becomes justified treatment. However, what about children born with ADHD? If we assume their untreated state to be normal, curing their disease would not be considered as treatment. There are, however, people who do agree that the norm should be the criterion, but who do not agree that ADHD should not be treated. Thus, we might

further generalize our notion of normality and say that normality is defined by the species' average. This implies that all measures aiming to establish a species-typical state would be considered as treatment, while measures aiming to improve an individual's state beyond the species average would then be considered as enhancement.

As mentioned above, allowing treatment and rejecting enhancement is a common position, and we have seen the range of actual positions spanned by this, depending on the definition of normality we apply. However, there are also positions that encourage enhancement. We strive to achieve above-average performance in different fields by so many means (like good education, special diets, meditation), proponents of such positions, like Arthur Caplan (2002), argue that it is not obvious why the goal of self-improvement should be illegitimate in the case of neuropharmacology.

In everyday life, actual positions are typically located somewhere between a liberal form of "treatment only" position, as held by Francis Fukuyama (2002), and positions favouring slight enhancements. Discussions like the one about Ritalin, or the case of plastic surgery in another domain elicit this conflict. Even within "treatment only" positions and when there is agreement on the type of normality to be achieved by treatment, a "species' average" is hard to obtain for something as complex as mental phenomena. In the case of Ritalin, for example, the boundaries between common childlike and pathological behaviour are fluid, resulting in a "grey zone" in diagnosis⁸. Still, we think that the existence of a continuum has become evident on which different positions can be located relative to each other.

The second dilemma we are facing in the treatment/enhancement debate is dealing with pressures that might arise to submit to neuropharmacological treatments. Whereas the first dilemma was dealing with the freedom to take certain substances, this dilemma is concerned with the freedom not to take certain substances. One end of a potential spectrum would be the principle

⁸ Furthermore, one might argue whether enhancement makes me not to be myself anymore – or rather to be even more myself? For example, is the real "me" the inattentive and nervous child or the disciplined and kind pupil?

that no one may ever be forced to take drugs against their will. On the other end, we would locate positions that justify forced drug use under certain circumstances (hormonal preparates for sexual criminals would be a prominent example).

There are more subtle pressures than legally enforced drug use, however. This leads again to a continuum of graded positions between the two extremes. To take up again the case of ADHD, the freedom of the individual to reject Ritalin is not reduced by legal standards, but by social pressures exercised by schools, parents, or doctors. In the professional world, there might arise situations as well where the rejection of enhancing one's performance can result in negative consequences. In such cases, one can imagine (at least) two different positions. One which will recognize the relevance of implicit pressures and therefore actively fight such pressures to keep up individual freedom, while the other position might find it sufficient to protect individuals from explicit pressure.

Let us present the axes arising from the discussion of the two dilemmas above.

Axis 1.1: Availability of Existing Means

Positions on this axis range from "no intervention for anyone" through "only treatment, but no enhancement" with increasingly liberal definitions of treatment to "enhancement for everyone".

Axis 1.2: Liberty of Denial

Positions on this axis range from complete rejection of forced use through different positions concerning implicit pressures to the acceptance of explicit pressure.

We started out in the hope that by designing such axes, we would be able to locate certain positions in the space spanned.

The Center of Cognitive Liberty and Ethics (CCLE) is well suited to relate other positions to, as its policy advocates principles located towards the liberal ends of both axis (Wrye 2002):

1. As long as their behaviour doesn't endanger others, individuals should not be compelled against their will to use technologies that directly interact with the brain, or be forced to take certain drugs.

2. As long as they do not subsequently engage in behaviour that harms others, individuals should not be prohibited from, or criminalized for, using new mind-enhancing drugs and technologies.

The first statement positions CCLE towards the liberal end of the “Liberty of Denial” axis, the second one also places them towards the liberal end of the “Availability” axis.

Francis Fukuyama, as a representative of another position, distinguishes treatment and enhancement on the basis of the purpose of medicine, such that treatment is to heal the sick whereas enhancement creates posthumans by “turning normals into god”. This places him on a more restrictive point on the availability axis.

We have kept this section specific to psychopharmacological substances. However, the positions here can be generalized easily to other, future forms of neurological interventions like chip implants.

Personhood and Personality

Personhood is a fundamental concept in our idea of man. It relates to the legal aspects of being human as it is closely tied to the awarding of rights. There is wide consent about the need to protect persons, which, however, results in heated debates about the exact definition. In bioethical border cases like abortion, cloning or euthanasia, the ethical discussion has evolved around the question whether the subjects in such cases could be called persons.

Personality is a concept distinct from, but related to personhood. For those individuals which we call persons, personality refers to their unique characteristics.

Neuroscience not only encounters similar questions like bioethics about human rights in border cases, but goes beyond these as its subject is the analysis and potential manipulation of the very foundation of personhood and personality: the brain. Changes to personhood and personality are both crucial points to investigate. But particularly interesting questions arise where both overlap, and where we have to judge whether we are facing a change of personality or whether we have to question the very possession of personhood.

In the near future, technology may enable us to perform surgeries to change certain aspects of personality. Let us construct our second case: Phineas Gage is a prominent example of personality change through physical manipulation of the brain. The manipulation, in his case, stemmed from an accident in which an iron pole destroyed parts of his prefrontal cortex. He survived this dramatic incident, but suffered from severe personality changes. In short, his ability or willingness to behave within social norms seemed distorted, particularly in contrast to his former traits of character. In a thought experiment, let us imagine Phineas Gage would live today and we were able to restore his original identity through psychosurgery. Would we want to justify such an intervention? Would he want such an intervention, and who is “he”, Phineas Gage before or after the accident? What if the new Phineas refuses the treatment although we can be sure the “old” one would have been happy to take that chance?

These questions are extreme variants of classical issues in medicine related to the notion of “Informed Consent”. Medical ethics requires health professionals to inform patients about the benefits and risks of a potential treatment, and to get their explicit, written consent before realizing the procedure. There are exceptions to this general guideline. Patients who are in a non-conscious state obviously cannot fulfil such requirements. In these cases, the proxies of the patient take over responsibility and go through the informed consent procedure for them. A less definite case would be the treatment of patients with Alzheimer’s Disease. Such patients go through different stages of this disease, with a continuous decline of mental capabilities. When the patient loses the ability to decide in his best interest, responsibility would have to be transferred to proxies as well. However, particularly in the complex context of medical treatments, this point in time is hard to assess.

The question why such a step could be justified brings us back to the question of personhood, which is particularly touchy when identity of personality over time is no longer given. The deciding criteria on which to grant or refuse personal rights are typically considered to be self-consciousness and rationality. Anyone planning to transfer responsibility from patient to proxies

would have to prove that these criteria are no longer satisfied.

Our example of Phineas Gage now sharpens these questions: In his brain-lesioned state, he is – just like before – self-conscious and rational, so there is no reason to take away personal rights from him. Yet, intuitively, we would argue in favour of restoring his old personality anyway because this is the one that has been Gage’s natural state in the absence of injury. So such an intervention would have to be considered as classical treatment and thus as justified even in more restrictive views like when normality is defined as the state in the absence of dramatic external influences (cf. the discussion on treatment and enhancement above). However, one might argue that changing Gage’s personality on purpose (an intervention which is not based on concrete medical needs but on a potentially biased view on desirable and undesirable properties) is ethically questionable. Even though we said that we favoured such treatment because it restores the original, would we really consider such a restoration if we subjectively judged the new person to be nicer? Particularly when the “new” Gage rejects such a treatment, who would be in a justified position to proceed nevertheless? If we were to adopt such a position, we would either have to find arguments why the new Gage cannot be considered a “full” person, or drop our principle of the patients’ self-determination and define reasons that override it. If we come to a point where it may be considered ethical to alter someone’s personality against their will (for example, by reducing their personal rights by doubting their full rationality), however, it is only a short step from restoring Gage’s old state to manipulating persons without brain damage, but with undesired behaviour. The legalization of court-ordered intervention on the level of the central nervous system could be a consequence.

Again, let us try to define an axis here on which to align the different views on this topic.

Axis 2.1: Persistence of Personhood

Positions range from standpoints insisting on personal rights for even severely impaired people through opinions legitimating denial of such rights in certain cases of personality changes to a position

that would even override “full” persons’ wills.

Privacy

Within the neurosciences there is a rapid emergence of brain imaging techniques enabling us to take detailed pictures of the brain. Methods like CT (using series of X-rays), MRI (measuring changes in blood-flow) and PET (detecting emission from radioactive material) have a widespread impact on neuroscience. They help to understand relationships between different brain areas as well as to assign their function. Functional MRI even allows for the monitoring of brain activity under different conditions and with that provides an anatomical and functional view. However, there still are far more questions than answers in the field of brain-imaging: What can we really get from these pictures with red and yellow colour patches on a grey background? What exactly do the variables represent? Is it justified to map the data on actual mental states? Nevertheless, the progress enabling us to get more and more data from what happens in the brain provides a more reliable foundation for diagnosis and also promises new kinds of applications.

Currently, the evaluation of data gathered by these methods relies on the statistical comparison across different subjects: Each brain is so unique that only trends in populations can be identified, while an individual brain remains hard to analyze so far. However, there are efforts to increase the interpretability of brain scans, for example the development of the Talairach coordinate system, which helps smoothing at least the topographical differences among different brains.

Let us construct a third case and imagine a future scenario where our ability to make definitive statements about individual brain states and to map such brain states onto mental states has advanced. Once this advance has gone far enough, it will enable us to engage in brain-reading. Thinkable applications lie in investigations in criminology, identification of traumata in psychotherapy, or even every-day private use.

Recently, there has been an example of using EEG techniques to improve reliability in lie detection (“brain fingerprinting”). In the study (Farwell 2001), a certain signal indicating strong affective response was evaluated. This was

combined with the presentation of seemingly irrelevant pictures. Some of these pictures, however, showed scenes or objects that were present at the scene of the crime. A suspect's connection to a crime would then be judged by the measured responses to those pictures who are only meaningful to someone involved. Even though EEG is not a brain imaging technique, but an earlier method for monitoring brain-activity, this already points at the potential ethical implications of future techniques providing ever more detailed insights: Is it acceptable to invade a person's (potentially even subconscious) mental states? How much should we trust such kind of findings?

Concerning the first question, the continuum of potential positions seems to resemble the "Liberty of Denial" axis found in the first case: Again, the question is how strongly the freedom of the individual to refuse an intervention is weighted in relation to the potential social benefits of a forced application. Concretely, it is the individual's privacy which is at stake, compared to the interest of prosecution or other causes presumed worthy.

The second question seems to span a new dimension. It deals with the attitude towards the trustworthiness of claims produced by technological progress in the neurosciences. Critics of any kind of technology that promises a link between physiological data and mental states could argue by the complexity or the transcendental nature of the brain that any such measures are doomed to fail. Proponents of such technology would stress the reliability of scientific findings validated by numerous means. Between those two extremes, we can imagine positions that acknowledge the benefit of modern scientific methods but still are aware of their relativity.

Looking back, many methods put to use by scientists centuries ago look naïve and misleading with today's knowledge although they seemed reasonable and well-founded in their time. For example, one might argue that although statistics is a very well-developed field, it can only give an answer to the questions one asks. In our case, what the EEG tests in the ideal case is if the subject has been at the scene of the crime, not if he/she is the criminal. Such kind of subtleties may seem

obvious now, but there is a risk they escape the public's notice when there is an important-looking machine promising simple answers.

More generally, whether the questions that are at the basis of neuroscientific experiments make sense is not provable in a mathematical way but depends on the prevailing valid paradigms. On the other hand, of course, this is the way of scientific progress and should not hinder us to embrace new technologies today. Still, embracing new technologies is one thing – trusting them so blindly as to rely on them in fundamental societal processes like prosecution is another. So there is plenty of space between the two extremes for a differentiated location of various positions.

This amounts to the following two axes:

Axis 3.1: Estimation of Privacy

Positions on this axis range from standpoints favouring the absolute value of mental privacy to those which rank higher the potential social benefits of invading it in certain cases.

Axis 3.2: Scepticism

Positions on this axis range from positions rejecting any validity of brain-reading techniques through different shades of sceptical positions to such which credulously embrace these techniques.

One concrete position towards the use of new neurotechnologies is the decision of the Iowa Supreme Court to admit the use of the aforementioned "brain fingerprinting" technique. This indicates a rather credulous position on the scepticism axis and little concern about issues of mental privacy.

Generalization

Until now, we discussed three cases and found several axes on which positions concerning these cases could be located. In the following, we will take a closer look at the nature of these axes and try to unify them into a single coordinate system. This idea was driven by the intuition that some axes go hand in hand in the sense that a certain position on one axis often implies a certain position on the other one. A short recapitulation of

the axes we found in the particular discussion of the cases:

- Axis 1.1: Availability of Existing Means
- Axis 1.2: Liberty of Denial
- Axis 2.1: Persistence of Personhood
- Axis 3.1: Estimation of Privacy
- Axis 3.2: Scepticism

We propose the following three general axes: “Liberty of Denial”, “Liberty of Use” and “Scepticism”. The goal in this generalization was to find a minimal set of axes which still provides enough expressive power to locate the relevant different positions in our “opinion space”. When we found correlations between two axes in the way mentioned above, we tried to collapse those onto one single axis representing the general continuum from which positions on the other axes could be derived. At the same time, we maintained different axes when we could identify positions which would be equal on one but different on the other axis. (cf. the first case in which we could imagine positions similar on the “Liberty of Denial” axis but different on the “Liberty of Use” axis).

Liberty of Denial

The most central issue in our analysis is the autonomy of the individual faced with the societal impacts of neuroscientific findings. Opinions range from absolute priority of personal rights to the relativization of these rights compared to other values. The autonomy to reject neuroscientific interventions (Axis 1.2) is a clear instance of this continuum. The privacy issue (Axis 3.1) deals with a similar question. The “Persistence of Personhood” axis (Axis 2.1) may seem a bit further away from the general axis than the two previous ones, as the discrepancy between the interests of an individual and authorities is not quite as obvious. But what is common to all of them, and why we decided to collapse all the three onto one axis, is their concern with the question of the power of society to interfere with individual decisions.

Liberty of Use

Another important axis concerns the availability of new achievements to the public. This became particularly evident in the case of treatment and enhancement (Axis 1.1) as it already is a practical concern how much liberty to grant to people concerning the use of drugs. Positions in general range from complete freedom to complete restriction. Although we didn’t discuss such an axis explicitly in the last two cases, we do recognize the relevance of this spectrum: In the case of privacy, we can imagine a point in time where mind-reading tools could practically be made available to the public. Would we then embrace a development where anyone can use tools like this in their private life?

In the case of personhood, the liberty of individuals to take the consequences of an altered personality might be rephrased as a legitimate claim. While there is no “usage” in the actual sense, the liberty to live through states of mental change might be considered a positive right as well. Opinions towards these issues seem to be located on the same axis like our initial one about the availability of neurological interventions by psychopharmacological means.

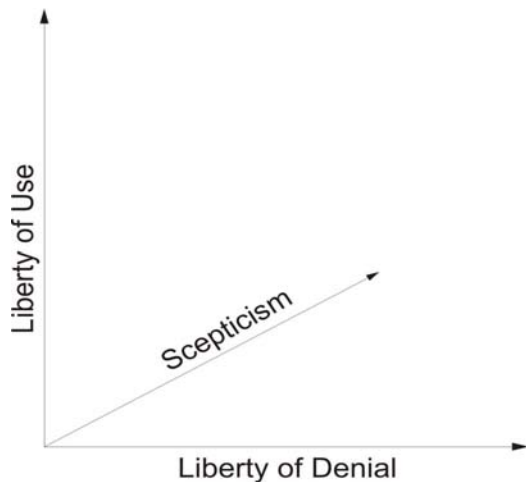
Scepticism

The final axis in our coordinate system deals with the general amount of trust towards scientific achievements. Positions on this axis range from complete rejection to credulous embracement. The axis we defined in the privacy case (Axis 3.1) within the field of brain reading can also be found in the field of treatment/enhancement: Of course, it is completely reasonable to ask in how far psychopharmacological drugs might help or maybe harm and also how secure one can be when taking the drug.⁹ Similarly, one may question the reliability of findings implying a reduced concept of personality. Again, one could, for example,

⁹ See Farah (2002) for concrete examples of potential dangers of extending mental performance. Increasing the number of items that can be kept in working memory, for example, might impair the ability to combine these items creatively. Such effects are non-obvious and might escape standard clinical testing procedures.

stress the importance to scrutinize scientific results when deriving dramatic consequences for individuals.

To sum up, we were able to identify three major underlying themes which lead to a three-dimensional space enabling us to locate all positions in all cases we examined:



A central finding is the existence of two independent concepts of liberty involved. Such a distinction is well-known in the political sciences. While it does not map onto the distinction between economic and personal freedom, it does map onto the axes spanned by the “Two Concepts of Liberty” made explicit by Isaiah Berlin (1969): Positive and Negative Liberty. Positive Liberty is equivalent to what we called “Liberty of Use”: It is a “liberty to” – speak freely, get health care, access existing resources at free will. Negative Liberty equals our “Liberty of Denial”: It is a “liberty not to” – follow common norms, embrace supposed advantages, have your private life influenced by authorities in general. A nice consequence of this parallel is the possibility to take advantage of findings Berlin made about the relation between these two axes and apply them to our domain. One such transfer is the conflict between the two liberties: For example, too much positive liberty, Berlin argues, may result in a restriction of negative liberty. Positive liberty easily leads to a situation where access to some resource gets such high priority that, in turn, social pressures arise that make it hard for individuals to realize their negative liberty and reject the resource.

Concerning our first case study, the recent abundant prescription of Ritalin to school kids (representing a positive liberty) creates an atmosphere in which the choice of parents in border cases (the negative liberty to refuse behaviour-altering drugs) is restricted.

In addition, we propose a further dimension, Scepticism, which is not found in political coordinate systems: It is special to concerns in philosophy of technology. We assume this axis not to be completely independent from the two liberty axes: Positions on the plane spanned by positive and negative liberty will be correlated to the position on the scepticism axis. It is hard to imagine a consistent position with both high positive liberty and high scepticism, e.g., providing free access to a drug without confidence in the benefit and harmlessness of it. On the other hand, the scepticism axes is not redundant either: We can imagine positions where equal positions on the liberty plane lead to different consequences depending on the position on the scepticism axis. For example, a state which would consider brain reading a legitimate legal practice in general (little negative liberty) may or may not arrive at actually using it, depending on the confidence in the new technology (high or little scepticism). Thus, we deem the postulation of this third axis justified.

Conclusion & Discussion

In this paper, we have proposed a general framework for ethical considerations in neuroscience. We started by motivating the particular field of neuroethics. We then presented three different cases to highlight a sample of emerging issues. For each case, we showed the variations among possible positions and proposed axes to account for them. In a final step, we found a unification of the specific axes to a generalized coordinate system. It consists of two axes representing the degree of estimation for two different kinds of liberty: The “Liberty of Denial” and the “Liberty of Use”. A third dimension is spanned by the degree of scepticism towards the new technologies.

We have shown examples in which the difference between two positions showed up on one axis only, while the difference could not be expressed by using the other axes. Although the

positions on the axes are slightly correlated, in the sense that not all positions in this space correspond to sensible opinions, this demonstrates that neither of these axes can be reduced to another one. Hence, we conclude that our proposed system has the minimum required dimensionality.

We will now briefly address a few questions which exceed the scope of this paper, but might be interesting to pursue further, particularly in dialogue with researchers active in the field.

First of all, the question arises whether our axes are correct. Do we need less, other or additional axes? Are axes the right format of conceptual representation after all? It will be necessary to review other subdomains of neuroethics (concerning, e.g., “neuro-marketing”, implications for education, or military usage) and test the applicability of our model.

Another task would be to fill our coordinate system with content. The location of a concrete position in the system is necessary both to test its validity and to turn it into a useful tool. Once standpoints in concrete cases are located, we can imagine that areas in the space emerge that can be assigned to general opinions regarding ethical questions. This might allow for the test of one’s current standpoints for consistency and also to decide between alternative standpoints in new cases, based on one’s general position in the space. Furthermore, one might go so far as to try to determine which choice of coordinates is best in a given situation, or even in general.

Such concrete applications, however, would have to be regarded with extreme caution. We do not want our system to be understood as an argument in favour of stereotyped thinking. Since standpoints can only be positioned relative to each other, an assignment of absolute values can only be an approximation. More generally, each case, of course, must be discussed on its own.

Neither do we want to implicitly encourage relativism: Not every position in our space can be accepted – a conclusion which might falsely arise from the neutrality of points in a space. On the contrary, we hope that the system helps to find the spectrum in which the discussion is reasonable and maybe even to define the borders to areas where it is not. If we have certain assumptions about human rights we never want to abandon, the point

where we do so might actually be put on an axis as the border we do not want to surpass.

We think our coordinate system could contribute to simplify and structure issues in the formation process of neuroethics. It is a good device to locate opinions relative to the extremes and to each other. For example, it might facilitate discussion if the difference between two standpoints can be summed up as a difference on the “Liberty of Denial” axis. So it could serve as a common language necessary in an interdisciplinary dialogue involving representatives from neuroscience, medicine, philosophy, law, policy, and sociology. Further, it might help in the societal task to bring into consciousness the consequences of brain-research.

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<http://www.transhumanism.org>

Part V

Conclusion

Summary

This documentation has given an overview over both the work processes taking place during the 18 month of the MINI project and the results of this work. Below, find a summary of each of the three major parts of the project, before we come to an overall summary of the project.

Affective Priming and Hemineglect

We developed a lateralized affective priming paradigm to research three experimental questions. First, the paradigm can test residual visual processing in hemineglect indirectly by means of demonstrating visually induced affective priming effects in the neglected part of the visual field in visual neglect. The paradigm presents affective pictures as primes in the neglected and the healthy visual semi-field. We expect to find affective priming effects due to affective pictures in the neglected part of the visual field, even if patients can not report having seen the stimuli. If an effect can be found in patients with neglect, it could be selectively attributed to early and automatic processing of visually induced affect, because affective priming effects with SOA under 300ms have been well established as early and automatic.

Second, our paradigm demonstrates an direct, qualitative influence of automatic affective processing on the perception of affective valence, as has been proposed in emotional theories for about two decades. We use an conscious affective valence evaluation task as response task in our priming paradigm. We could demonstrate a negative rating bias for affectively neutral target pictures that were preceded by negative primes, thus demonstrating that automatic affective processing of the prime influences explicit valence evaluation of the target picture.

Third, the paradigm can be used to research lateralization of affective priming. By lateralized presentation of the primes, we evoke automatic processing of affect separately in each hemisphere. Unexpectedly, we found a hemispheric difference due to neutral primes, rather than due to negative or positive primes. Neutral primes presented to the right visual hemi-field (that is, the left hemisphere) lead to more negative evaluation of neutral target stimuli than right hemispheric presentation of neutral targets. This finding might reflect a baseline difference in the processing of affect between the hemispheres, such that stimuli in the left hemisphere are evaluated more negatively than stimuli in the right hemisphere (following the valence hypothesis on emotional lateralization). However, such a baseline difference may not be strong enough to

substantially influence highly emotional priming stimuli (either negative or positive) in a significant manner, so that the baseline might show only with affectively neutral primes.

The virtual Morris Water Maze

The part of the project concerned with spatial navigation was mainly focusing on two issues: Firstly, we wanted to know if there is a lateralization of hippocampal function, and secondly, we were interested in the basis of observed sex differences of spatial navigation.

Regarding the first issue we present an overview on the theoretical background of spatial navigation in the documentation. Specifically, we review literature that is providing the case for an prominent involvement of the hippocampus in tasks of spatial navigation fostering the reliance on allocentric (vs. egocentric) representations of the environment, such as way-finding in complex labyrinths and place learning restricted to distal cue use. Thereby it becomes clear that the current state of affairs in this area is rather controversial when it comes to a possible lateralization of spatial and verbal mnemonic function of the right and left hippocampus respectively. To contribute to the clarification of these controversies we were preparing a patient study employing the virtual version of the Morris water task.

Regarding the second issue, the basis of sex differences in navigational ability, we prepared and conducted a study with the virtual Morris water task. We found that men are faster than women in learning the position of a hidden platform, which is concordant with other studies exploring navigational behavior for both genders. However, we could also show, that men are more affected by interleaved non-stationary platform trials, which reduced the difference between the genders to an amount that rendered them non-significant. We interpreted these results in the context of mental representations built of the environment. Specifically, we argument that women tend to use egocentric representations, while men are rather likely to rely on allocentric representations when navigating through unknown environments.

Additionally, virtual reality as a tool in cognitive assessment is introduced, and limitations and advantages are discussed. For the research field of spatial navigation we specifically deal with the validity of scientific methods based on virtual reality and with threads to it.

Neuroethics

We argued for the importance of work in the intersection of ethics and neuroscience. Neuroscientific knowledge has theoretical implications for fundamental anthropological and ethical concepts, and ethical criteria have practical implications for neuroscientific undertakings (ethics of neuroscience).

We encountered the practical consequences of ethical considerations when we tried to get the admission to carry out experiments with patients. It was interesting to see how the realization of the ethical standards we value so much in theory turned out to be a tedious obstacle in practice, particularly because they were applied inappropriately concerning the biomedical research questions. This dilemma between idealist thinking and practical considerations, looking back, does in fact in itself constitute a valuable experience within the project.

In the article “A Framework to Systematize Positions in Neuroethics”, we discussed three cases around the topics of treatment/enhancement, personhood and privacy, and we generalized the resulting possibilities to position oneself. We arrived at a three-dimensional coordinate system spanned by the axes of “Liberty of Denial”, “Liberty of Use” and “Scepticism”. With this, we hope to provide a common language simplifying interdisciplinary dialogue and communication with the public.

General Summary

Starting from the general possibility to collaborate with the neurosurgery at Osnabrück’s Paracelsus Hospital, the members of the MINI project have created two research questions fitting the hospital’s patient population and designed suitable paradigms, both of them using innovative experimental tools. These paradigms have been implemented and applied to student subjects. Two resulting articles proof their suitability to tackle interesting neuropsychological questions. Additionally, general questions regarding the ethical implications of neuroscientific progress were pondered, which led to a third article.

Delays in the approval process obstructed the execution of the experiments with actual patients within the time frame of the project. As this documentation is finished, however,

everything is ready to begin testing patients. So beyond the scientific results of the project, the very general goal of paving the road for and establishing a cooperation with the Paracelsus Hospital was achieved, and hopefully further study projects will take advantage of this possibility.

Evaluation

Scientific

Find research hypotheses

Constraints of the patient population

- Found two interesting, different themes compatible with potential patient population.

Develop literature background

- Collected and became familiar with a large body of relevant, current and central work in hemineglect and affective priming, spatial navigation and neuroethics
- ❑ Organization and distribution of relevant information (finding out what's important and getting it into everyone's head) turned out to be difficult. We should have documented the purpose of each article, to read with more purpose.
- ❑ Our library proved limited for neuroscience and we often had to seek resources elsewhere.

Adapt to new constraints

- Reformulated the two research questions for a healthy population while waiting for the legal situation concerning the patient study to be resolved.

Develop paradigm

Understand and select design principles for neuropsychological experiments

- Designed two experiments within our selected paradigms.

Implementation

- Built an open source XML compliant customizable precision-timed program to test affective priming.
- Customized an existing virtual reality 3-D first person perspective program to test our research hypothesis in spatial navigation.

Carry out experiments

Develop competence in clinical environments

- Prepared a protocol for patient interaction.
- Were able to observe brain surgery and get accustomed to the clinical setting. Furthermore, this allowed us to empathize with them more than from only reading about pathologies.

- ❑ Did not have the opportunity to obtain practical expertise in clinical environments due to delays in receiving approval for our experiments from ethics boards.
- Our gained expertise will facilitate future interactions between people involved in the Cognitive Science program and the medical community in Osnabrück.

Develop competence in conducting experiments

- Gained experimental practice through carrying out the experiments with students.
- ❑ Carrying out the experiments was hindered by the lack of experimental infrastructure, like a room for graduate students' experiments.

Output

Analysis

- Deepened our knowledge of the concepts of statistics and learned to apply them to our experimental data in the SPSS data analysis software.
- ❑ Those team members not directly involved in the data analysis did not get as much experience in statistical methods.
- Interpreted results against background of current literature.

Presentation

- Created three independent articles for submission
- Justified our work in front of the members and students of the insitute during a presentation of our project.
- Recorded our experiences and results in this documentation.

Contacts

- Established an infrastructure for cooperation with the Paracelsus clinic, and potentially others.
- Contacted different researchers for research material.
- Got materials and support from the Neuroethics group at Stanford.

Administrative

Project Organisation

Teamwork

- Gained practice at general soft skills.

- Practiced moderating of sessions, giving feedback, motivating
- Learnt how to pass on results of single work in summary form to team members.
- Managed intercultural and other social challenges.
- Working atmosphere was open and yet professional – allowing a self-organising group structure as opposed to a typical hierarchical student situation.
- ❑ Strong central control might at times have rendered things less interesting but maybe more efficient.
- ❑ Dependencies between project components were not always clear.

Labor division

- ❑ Unequal distribution of workload and responsibilities.
- Learnt what to focus on when dividing workload into components.

Tools

StudIP

- ❑ Lost time, energy and nerves searching for basic functionality like sorting files by date, creating folders etc.
- Used StudIP for document exchange rather successfully once these issues were settled.

Web page

- Created a dynamic web page for coordination and presentation to the outside.
- ❑ Internal use was limited.
- Provided exposure and resulted in several contacts.

Establish cooperation with the clinic

Identify legal issues

- Got acquainted with procedure of ethic reviews.
- Prepared an application to get approval from an ethics committee, presenting research hypothesis in an appropriate manner.
- Successfully resolved a dispute with an ethics committee with the help of a legal advisor.

Contact

- Established an inspiring and exciting working relationship with professionals in the field outside the university: The neurosurgeon Prof. Dr. Albert at the local Paracelsus Clinic.

Outlook

The MINI project has officially ended now. We finished our experiments within a student population and wrote papers and documentations about it, as well as a paper on neuroethics. Our supervisor Jacqueline Griego has returned to work in the USA.

However, some of the project members are looking forward to continue the research that we already prepared. Now that we have the agreement of the ethics committee to conduct experiments with patients with cerebral damage, we will be able to realize our original experimental intentions, and possibly some of us are going to write their Master's thesis about it. In general, we hope to have established a cooperation between the Paracelsus Clinic and the University of Osnabrück that will be fruitful also in further research and study projects. The integration of experimental work and interaction with brain surgery patients can be a valuable experience during an otherwise more theoretical study approach in the field of neuroscience.

Hemineglect and Affective Priming

We are now starting to carry out the experiment originally designed. Should the experiment succeed, further research could vary various parameters: the stimuli being used, the prime presentation time, the SOA. One larger aim of this line of research is to come to a conclusion on the nature of visual neglect. That is, at what level of visual processing does the impairment in hemineglect occur? This would mean to work out what complexity in visual processing is required for automatic affective processing to occur. Which means to investigate what features of the visual stimuli need to be extracted, and to what level, so as to induce affective priming on visual stimuli. Given this knowledge, one could conclude that the respective processing is intact in the hemineglect syndrome.

Concerning the hypothesis on the qualitative influence of automatic affect processing on conscious perception of valence, one larger aim were to replicate studies on the automatic nature of affective priming in the qualitative kind of priming paradigm used here. This would mean to vary the paradigm with different kinds of stimuli and target tasks, and to vary the SOA. As in affective priming paradigms that assess response latencies rather than change in the qualitative content, increasing the SOA should lead the effect to disappear, and decreasing SOA to subliminal presentation times still should evoke an effect.

Concerning the research question on lateralization, two further lines of development lie at hand. The first is to enhance the lateralization procedure to increase the fixation of the central fixation mark, so as to avoid orientation responses towards the appearing primes. One way of doing this were to increase the saliency of the fixation mark relative to the saliency of the primes. Another way of doing this would be to present the primes for time shorter periods than visual saccades need to be performed. Yet, the most reliable ways to ensure lateralization were to use a classical Z-lense as used in the Split-Brain experiments, or an eye-tracking device to present the stimuli lateralized depending on the current position of the eyes. The second development is to vary to investigate the processing stage at which lateralization occurs, and to vary the kinds of target stimuli. That is, to lateralize the targets in addition or as alternative to lateralizing the primes, and to include positive and negative stimuli in the target sets.

Spatial Navigation and Hippocampus

Concerning the investigations in spatial navigation, there are two issues to be addressed. Regarding the Morris water maze experiments with hippocampus patients the stage of affairs there is similar to the affective priming experiments with patients suffering visual neglect: We finally obtained the permission from the ethics commission to conduct the experiments with patients with hippocampal damage. Therefore our immediate aim is to get some patients helping us. As already discussed in the documentation, we will try to reproduce the finding that unilateral right, but also unilateral left hippocampal damage significantly impairs the performance in the MWT (Astur et al., 2002). We will examine which role the lateralization of the hippocampus plays: does damage to the left hippocampus affect the spatial abilities in a different way than damage to the right hippocampus? Is possibly only one hippocampal hemisphere, that is the right, crucial for the navigation in tasks requiring, or at least fostering allocentric mapping? A clarification of these questions can only be reached, when the study outcome is unequivocally interpretable. In this sense it is that these experiments require subjects who suffered damage relatively restricted to the left side of the hippocampus as well as subjects who suffered circumscribed right hippocampal damage. Finding and recruiting enough of those subjects will be one of the major difficulties in this experiment and may take some more weeks or months.

Furthermore, it may be conceivable to conduct imaging or EEG studies with healthy subjects solving the Morris water task. To my knowledge, this would be something new, though many

studies explored brain activations in other spatial navigation tasks as complex labyrinths. Besides to be another means to explore the neural correlates of spatial navigation, such experiments would coincide with the second part of our interest in spatial navigation: sex differences.

In our experiment we could reproduce the sex difference found before in similar studies (Astur et al., 1998). Furthermore, it was shown that interleaved non-stationary platform blocks differentially affect men and women in their performance. This outcome can be interpreted as both genders using different mental representations of the space navigated. To supplement our investigation of the basis of the sex difference, the before mentioned imaging or EEG studies could prove helpful. Specifically, it would be interesting to know, if there is a tighter relation between sex and differential brain activations or performance and differential brain activations. It is possible to imagine that the use of differential representations we identified as the cause of the behavioral differences observed, is itself caused by differing abilities to process the spatial information. The borderline between these variations in ability may not be congruent with that dividing the genders (besides being less discrete).

Besides brain activation, cue use may be a marker of the representation used. Assuming the use of geometrical cues to indicate the reliance on allocentric representations, and distal cue use rather than on egocentric representations, it would also be interesting to change the type of spatial cues that are provided. The subjects could be forced to rely on geometrical cues instead of distal ones, for example the pool might be trapezoidal-shaped instead of round, thereby providing information about location. If the vanishing sex difference is based on distinctive representations, signaled by the distinctive use of geometrical or distal cues, it should not be observed when both genders are forced to use the same kind of representation. Besides this we would expect that the overall sex difference enlarges, as women are assumed to have more difficulties in using geometric information.

However, as computer and 3D-game experience were showed to have a strong influence on navigational performance in our experiment, a more urgent issue for future studies would be to eliminate this influence. On the other hand, a more sophisticated assessment of these influences could also be helpful in delineating the contribution of the independent variable gender on navigational abilities.

Neuroethics

Concerning neuroethics, more work needs to be done in order to develop general guidelines for dealing with the emerging issues. We hope to be able to further pursue the ideas laid out in the neuroethics article to help create an interdisciplinary language: Many fields will need to work together in the future more than they do today to deal competently with the social and legal consequences we are facing.

Afterward

Some months have passed since the official end of MINI. However, with the coordination efforts of Saskia Nagel and volunteer members of the project, Nicolas Neubauer, Frank Schumann, Christian Mühl, Stan James, patients from the Paracelsus-Klinik are finally participating in the Affective Priming and MWT paradigms!!! We from MINI are grateful for these individuals who, facing sub-optimal life events for them, volunteer their time and participation. We also give special thanks to Prof. Dr. F. Albert for this continued interest and support in the research started in the MINI project. As a researcher and teacher I am continually impressed by the ability of these M.Sc. students to do independent research and carry on developing their own interests and skills outside the boundaries of their programme requirements.

Jacqueline Griego

Baltimore, 2005