Spatial Cognition in Dynamic Environments

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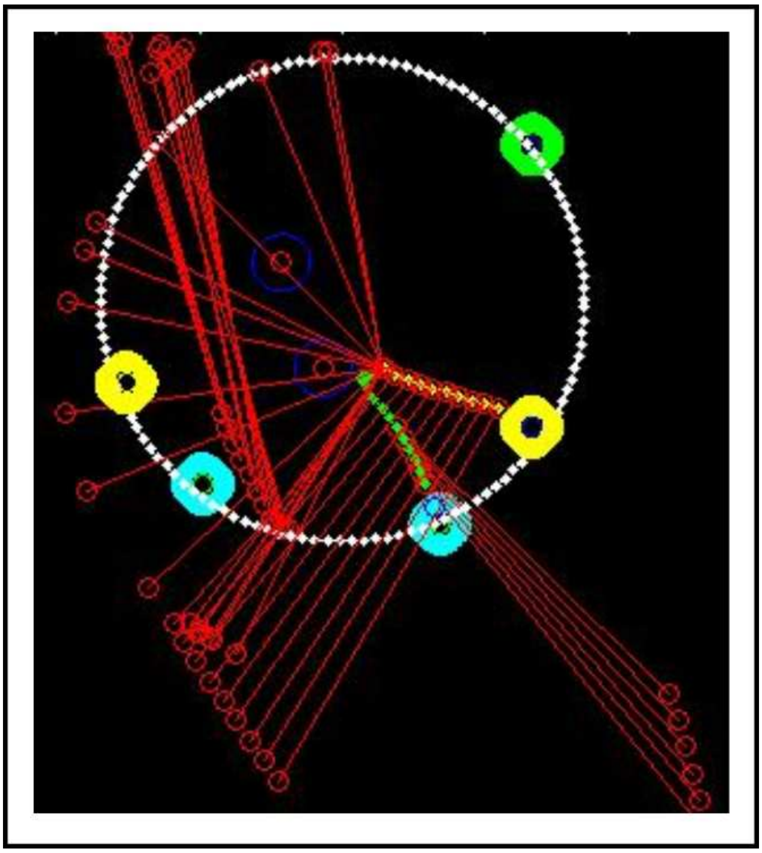
I would also to express my gratitude to my wife Marcela for her support during writing this thesis. I also want to express thanks to my first teacher of biology, Josef Pavlik, who initiated my interest in the natural sciences.



“**Dynamic space**”

(*Accidentaly created during analyses done for this thesis*)

Contents

Part I

General Introduction

World around us is not stationary but highly dynamic. In natural habitats, animals react to moving objects or subjects, e.g. to members of the same social group, sexual mates, preys and predators. Similarly, human world is full of dynamic changes; from a long past history humans were hunting the prey, fighting, or more recently playing ball games, driving cars and flying in the airspace. In a figurative sense it is possible to describe human activities as a dynamic "catching of everyday responsibilities" or a dynamic interaction with other beings and things in continuously changing social network. For successful survival in such complicated environments, animals and humans must be equipped with individual suitable adaptation mechanisms which had been created during evolution. It is important for many species to perceive efficiently stimuli from the environment on one side and to process the perceived information adequately on the other side. Cognitive mechanisms processing incoming sensory inputs in dynamic environments compute and code for not only spatial relations, but also spatiotemporal changes.

Despite intense research into the spatial behavior and place navigation, most of experiments done in animal species and humans exploited stable world conditions. In general, we can ask if living organisms perceive and process stable and dynamic world in the same manner. We can also search for differences of navigational strategies employed in either dynamic or stable worlds. Moreover, yet unanswered question is, which variables are processed during efficient navigation in the moving world. Which brain structures are important for neural processing of the stable or moving world? Are these brain structures different or do they overlap? Contemporary and past literature dedicated to behavior with respect to moving goals shows that a wide variety of experiments in dynamic (i.e. moving) environments was performed in various animal species and humans. However, only a few of them used rats as a model species. Nevertheless, rats are extremely useful model animals for studying relationships between particular behaviors and responsible brain structures. Other neurophysiological approaches and their potential in preclinical and translational research should also be taken into account.

The present thesis consists of several studies engaged on cognitive abilities of rats exposed to various types of dynamic and mobile environments.

The first study (Blahna K, Svoboda J, Telensky P, Klement D: Inertial stimuli generated by arena rotation are important for acquisition of the active place avoidance task, 2010; Behav Brain Res) shows the crucial role of the presence of inertial stimuli in rat's spatial learning. Participation of authors: Karel Blahna - conceiving main idea and design of main part of experiment, data analysis, writing the article, administration of the final experiment. Daniel Klement – co-partner in conceiving main idea and design of main part of experiment, data analysis, writing the article. Jan Svoboda - development of the previous important pilot experiments, administration and analysis of prefinal experiments. Petr Telensky- participation on development of the experiment, participation on writing the article.

In the second study (Telensky P, Svoboda J, Pastalkova E, Blahna K, Bures J, Stuchlik A: Enemy avoidance task: a novel behavioral paradigm for assessing spatial avoidance of a moving subject, 2009, Journal of Neuroscience Methods) we designed a new behavioral task for testing navigation abilities of rat with respect to another moving subject. Participation of authors: Petr Telensky - conceiving main idea, design of main part of experiment, data analysis, writing the programs for tracking the animal, writing the article. Jan Svoboda - design of main part of experiment, data analysis, writing tha article. Eva Pastalkova - together with Dr. Jan Bures administration of previous pilot experiments. Karel Blahna - participation on development of the experiment, administration of behavioral experiments, participation on writing the article. Jan Bures – initiation of the original idea of moving reference frames. Ales Stuchlik - coordinating the study and writing the publication.

Third study (Telensky P, Svoboda J, Blahna K, Bures J, Kubik S and Stuchlik A: Functional inactivation of the rat hippocampus disrupts avoidance of a moving object, the paper is currently under review in the Proceedings of National Academy of Sciences of the USA) shows that rat hippocampus is necessary for flexible spatial behaviors during navigation with respect to moving visible goal (a programmable robot), and that hippocampus is not necessary for estimation of distance to a stable visible goal. Participation of authors: Petr Telensky - design main part of the experiment, writing the programs for tracking the animal, administration of the experiment and participation on operations of the animal. Jan Svoboda - design of main part of experiment, overall analysis, participation on operations of the animals, Karel Blahna - participation on creating design of experiment, administration experiment and operation of animals. Jan Bures - conceiving to main idea, participation on writing the article. Stepan Kubik, Ales Stuchlik - participation on writing the article, scientific leadership.

Forth study was written by Daniel Klement and Karel Blahna (How can rat navigate toward the moving target?) This study was already presented in several foreign conferences and is currently under review in the Journal of Experimental Biology. Authors describe fundamental behavioral strategies of rats navigating toward the moving target in this study. The authors first described some hypothetical variables which might be important for sensation of the moving target by the rat. The authors also showed critical time latency 200 ms in which animals react to these parameters. Both authors had equal participation on designing, administration and analysis of the experiment and also writing the manuscript. Selected problems of interception of moving targets by rats and other animals were also published by the authors Karel Blahna and Daniel Klement in this article: Algoritmy navigace na pohyblivé cíle: Aneb „od Mouchy ke Schizophrenii“.Psychiatrie, (2008, Suppl. p 15-19).

Fifth work was published in 2008 (Svoboda J, Telensky P, Blahna K, Zach P, Bures J and Stuchlik A: Lesion of posterior parietal cortex in rats does not disrupt place avoidance based on either distal or proximal orienting cues. Neurosci Lett (2008). Here the authors evaluated the role of the posterior parietal cortex in environment which was dissociated into the two independent reference frames, defined by either proximal or distal cues. The authors have been showed that posterior parietal cortex does not play any important role for navigation in this type of dynamic environment. Jan Svoboda, Petr Telensky, Karel Blahna – performing the experiments, co-initiation of the main idea, data analysis. Petr Zach – histological evaluation of lesion. Jan Bures and Ales Stuchlik, coordination of study, writing, scientific supervision.

Sixth work covers a minireview, in which the authors Daniel Klement, Karel Blahna and Tereza Nekovarova summarized selected experiments done in the Department of Neurophysiology of Memory at the Institute of Physiology AS CR, v.v.i. This minireview in part complements the introduction of this thesis. All authors contributed equally to this work. All papers and manuscripts related to this thesis are enclosed after the main text and listed in the references (together with impact factors).

Chapter 1

Compendium of the spatial behavior

1.1 Behavioral aspects of navigational processes

"Navigation itself could be defined as a process of determining and maintaining a course or trajectory from one place to another" (Gallistel 1990). Various animal species must orient and navigate in different types of environments. In spite of the fact that different animal species are equipped with their own sets of perception abilities, they share some "common" types of navigational strategies. When an animal navigates, it can perceive prominent navigation cues in the environment and it can use them by different ways. Animal can remember that a prominent landmark is situated in the goal place, and in this case, it is sufficient to navigate toward a landmark (O'Keefe and Nadel 1978, Gallistel 1990). When a goal position is located in the environment with larger set of cues, animal can extrapolate goal location from their mutual spatial relationships (originally from Tolman, 1948). Another alternative approach to navigation is remembering set of consecutive motor actions, e.g. when the animal is already navigating from the same fixed starting position (Carr and Watson, 1908).

On this basis, O'Keefe and Nadel (1978) defined two basic navigational strategies: First, route-following navigation is characterized by usage of landmarks as beacons when navigating toward or away from them. In the second strategy, called mapping navigation (or cognitive mapping), animals use a set of landmarks as a “whole” for computing a path (Tolman 1948, O’Keefe and Nadel 1978, Gallistel 1990). Beside this division, different classifications of navigation were also proposed. These classifications were derived from the nature of stimuli that animals use for navigation (Gallistel 1990, Bures et al.1997a, Etienne 2003) or on the way, how animals respond to these stimuli in their natural environments or in laboratory conditions (Jeffery, 2003). Stimuli, which are generated during active animal´s movement through the environment, are called self-motion stimuli. However, motion stimuli can also be generated from a passive movement of the animal, such as rotating it on a circular platform. Navigation based on these stimuli is called idiothetic navigation. When animals use external cues, it is called allothetic navigation.

1.1.1 Taxis and Route-following navigation

Taxis is a primitive form of navigation, which is dependent on a presence of some stimulus or continuously increasing unimodal sensory (e.g. olfactory) gradient. Animals learn simply to follow or avoid some stable or moving stimulus in the environment. More frequently, animals can follow a set of sensory cues and respond to each of them by the appropriate behavior. This behavior is based on an instruction or a list of instructions which is/are bound to discrete source of spatial information and is called route-following navigation (O’Keefe and Nadel, 1978). Based on character of the instruction, it is possible to divide this strategy into two types of behavior: First type, guidance instruction, tells to the subject: “Follow, approach or avoid some object”. Second type, orientation instruction, instructs the subject: “execute a specific behavior, when a specific cue is presented”(see to examples in Table 1.1, and Figure 1.1.1)(O’Keefe and Nadel, 1978, Gallistel 1990, Jeffery 2003). In the route-following navigation, animals do not explicitly perceive spatial relationships of the whole environment, but they could perceive only its particular fragments which are bound with specific cues or ther set. This strategy is advantageous mostly in a familiar environment, but is not flexible, when some unexpected event occurred or when the animal was in

Guidance instruction		Orientation instruction	
allocentric	*egocentric*	*allocentric*	*egocentric*
"Go toward (or in opposite) side of the environment with a tree on the mounteen."	"Walk along a river until meet a tree and than turn left."	"Go toward a hill and when you see a lake in the valley turn on a right side and continue wolk on the direction toward tower situated on the hill. "	Go toward a tree on the hill and after going 100 m turn right and go 10 m in advance.

Table 1.1: *Examples of route-following navigation. Adapted from Jeffery et al. (2003)*

a new environment (O'Keefe and Nadel 1978, Jeffery 2003).

1.1.2 Mapping (locale) navigation

Edward Chase Tolman (1948) first proposed a controversial idea that possession of a complex cognitive map allowed an animal to correctly choose a new route when subjected to a new environment (see also Jeffery 2003; Thinus-Blanc, 1988). The concept of cognitive map postulated by Tolman corresponds roughly to the so-called topographical map (Baker, 1984), where animals use navigation arrays of familiar cues in a process called "pilotage" (Bingman 1998). As mentioned above, O'Keefe and Nadel (1978) divided navigation into a taxon system, which involves following of a sequence of landmarks along a route, and locale system based on construction of mental representation of spatial relationships between the landmarks (O'Keefe and Nadel 1978). According to their point of view, mapping navigation is not strictly dependent on a single cue, but rather involves "computation" of locations of the goal place from the configuration of the whole set or array of cues in the environment. When a cue is removed, the animal is still able to find a goal. Mapping navigation is very flexible; it is not disrupted when some part of the environment is changed, or when an obstruction or obstacle in the path is present (Gould 1986, Menzel et al. 1998, Wehner and Srinivasan 1981, Tolman 1948, Zandorfi and Poli 1970, Granon and Poucet 1995, Matthews and Best 1997).

1.1.3 Idiothetic (egocentric) navigation

During navigation, animals move actively or they can be transported passively. The movement generates perceptible changes in proprioceptors, tactile receptors and statokinetic inputs from a vestibular system (Gallistel 1990). Other types of information may be processed as e.g. optic flow from the visual system or so-called efferent copies of motor commands. These sensations result in detection of linear or angular changes of position of the body or its parts in the environment. Particular sensory signals are remembered and together with efferent copies from movement, they constitute a basis for navigation in the environment, which independent of external sources of information (Mittelstaedt and Mittelstaedt 1980, Etienne 1988, Gallistel 1990, Jeffery 2003).

A process, in which actual and remembered pieces of information from perception and motor efferent copies are integrated and stored, is called path integration (PI) (also known as dead-reckoning behavior) (Etienne and Jeffery,2004). Previously, some authors used a term analogous to path integration, "inertial navigation" model (Darwin 1873, Barlow 1964, Mittelsteadt 1983). Presupposed relationships between sensory inputs (based mainly on inertial inputs as vestibular information or information from proprioceptors and tactile receptors) and motor outputs allow an animal to maintain an internal cognitive map about its positions in environment (Taube, 2007). Recently, Wallace et al. (2008) have proposed fractionating PI into a compass system, which is involved in deriving directional information, and odometer system, which is involved in estimating distances from self-motion cues. In the next section 2.0.6, the role of the so-called inertial inputs will be discussed in relation to one of the remarkable forms of path integration, the dead reckoning (or homing behavior).

Other types of idiothetic navigation were also described beside path integration. Praxis navigation is a simple form of navigation, where animals or humans learn consequently an ordered set of proprioceptively-guided automatic responses (Carr and Watson, 1908).

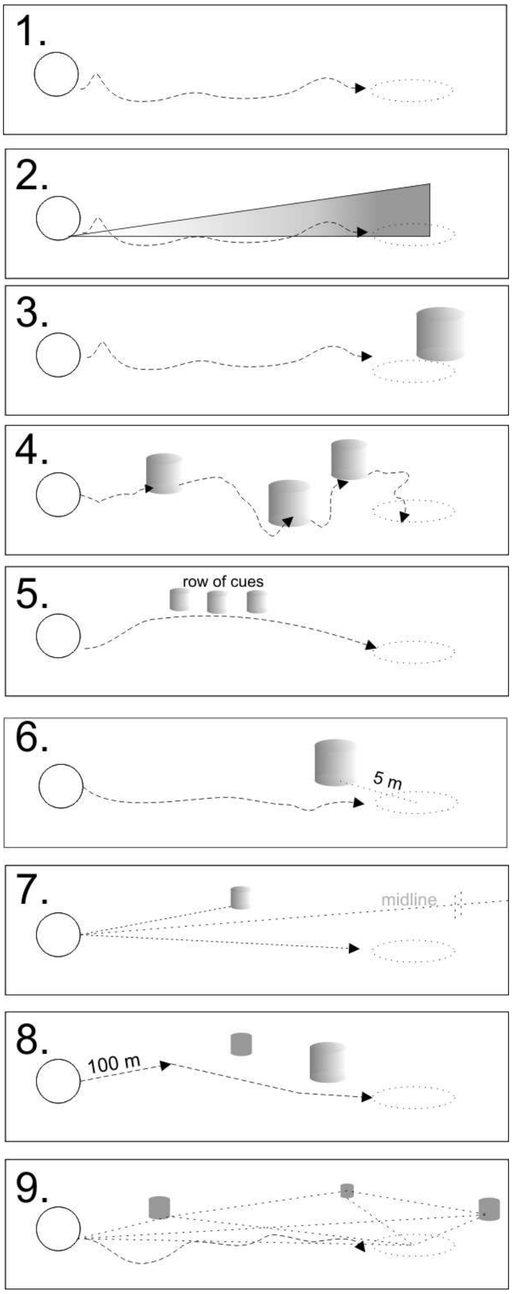


Figure 1.1.1: *Scheme of selected navigational strategies. 1: Subject uses egocentric strategy without orienting cues in the environment. 2: ERF strategy: subject approaches the goal place along a sensory gradient. 3: ERF, Taxis - subject approaches the goal marked by a salient cue. 4: ERF strategy: Subject goes from one cue to another. 5: ARF + ERF strategy: Subject navigates toward a row of cues (ARF) and then continues along a row of cues and then turns right (ERF). 6: ERF strategy: Subject use a proximal cue for estimating goal position, which is situated at some distance from the cue. 7: ARF strategy: Subject responds to the distal cue by going to opposite side than the cue. 8: Combination of ARF and ERF. Subject navigates 100m towards a distal cue and then turns right. When the subject approaches the proximal cue, it executes a small turn toward the goal location. 9: Allocentric strategy: Subject estimates position of the goal location from mutual configuration of cues inside environment. ERF - egocentric route following, ARF - allocentric route following. Inspired by Jeffery (2003) and Klement (2005)*

1.1.4 Allothetic (allocentric) navigation

Allothetic navigation is a form of navigation, in which animals use external cues for searching location of goals in the environment. Based on the way of stimuli processing, it is possible to divide allothetic navigation in several subtypes, which were in part described in the Table 1.1 and Fig 1.1.1).Taxis directed toward a distal landmark is the simplest form of allothetic navigation. 2) Route navigation in the environment with distal landmarks uses instructions to control of the body movement with respect to distal landmarks (a compass strategy). Animals can operate with a set of familiar distal landmarks inside 3) a known area (or so-called fragment), or they can 4) move between two known areas through an unknown area by using a knowledge about landmarks from both familiar areas. Processing of allothetic information is related to other types of spatial behavior described later in this thesis (Jeffery et al., 2003, Gallistel 1990).

Scene recognition

Scene recognition is a system for recognizing familiar places in the landscape. In insects, this system was characterized as a “snapshot” or a “view-matching” system (Cartwright and Collett 1982). Insects like bees store a viewpoint-dependent representation like particular snapshots from surrounding environment. Insects do not obviously construct Cartesian map of space but tend to move so to find a learned view-points from the familiar environment (Cartwright and Collett 1982; Collett and Cartwright 1983). This behavior has been also described in rodents (Buresova et al. 1985, Klement and Bures 2000). Hamsters naturally explore objects presented in new configurations, but such detection is altered when the animal enters the environment from novel vantage points (Thinus-Blanc et al., 1991). Scene recognition is useful in most familiar environments but it fails when some changes with configuration of distal landmarks occurred. Next part of the introduction2.0.6will also overview data showing the cooperation between scene recognition behavior and idiothetic information.

Reorientation

The navigation is sometimes interrupted by impingements from the environment and a new process of navigation must be activated. Such reorientation is a flexible process, involving the systems of path integration and scene recognition, which restores the representation of the spatial relationship between the animal and its environment when the path integration is fully disrupted (Jeffery 2003). Cheng and Gallistel (1984) proposed that reorientation in rats is based mainly on geometrical shape of the environment and not on the particular salient cues, but recently, some experiments have raised doubts on using a purely geometric module in rat navigation and rather supported so-called view-based model (Cheng 2005).

1.2 Overview of selected neural systems representing spatial navigation

This section will present selected brain structures related to processing of spatial information. As shown previously, spatial information is represented by external landmarks and information from vestibular, proprioceptive and tactile receptors and efferent copies of motor commands. This section will first focus on processing of spatial information controlled by external cues. Subsequently, more specialized sections of the thesis will also show engagement of brain structures in processing of other types of information.

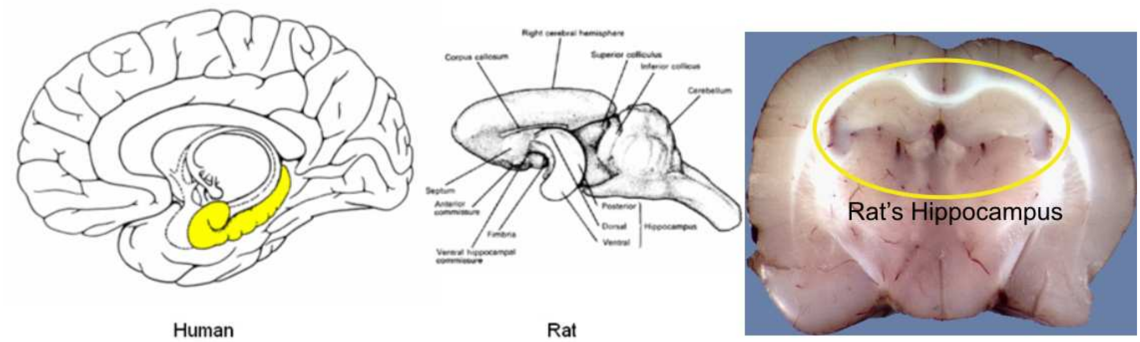
1.2.1 System of hippocampal place cells

Hippocampus is known as a structure involved in processing of spatial information especially related to “locations” as well as episodic form of declarative memory (Scoville and Milner 1957, Squire and Cohen 1984). This was first shown in the well-known case report of amnestic patient H.M., who underwent bilateral lesion to the medial temporal lobe including hippocampus for intractable epilepsy. After surgery, his memory and spatial abilities were strongly altered (Milner et al. 1998 for a review). O'Keefe and Dostrovsky (1971) first described that firing properties of hippocampal pyramidal cells, so-called place cells, correlate with actual location of an animal in the experimental environment. Subsequently, other pyramidal cells with specific characteristics of their firing patterns were demonstrated. These include border cells (Solstad et al. 2008) or misplace cells (O'Keefe 1976; Fyhn et al. 2004), which represent examples of neurons whose firing activity has a subtle but tight relation to the environmental features. Moreover, all these and other cells may contribute to the creation of neural representation or the map. Hippocampus is functionally and anatomically interconnected with many cortical and subcortical regions of the brain. The main cortical input that is interconnected with the hippocampus is entorhinal cortex, which provides main principal afferentation to the hippocampus (Ramón y Cajal 1893).

Anatomy of the hippocampus

Hippocampus is a bilateral brain structure situated under the neocortex in rats and deep inside the temporal lobe in humans (see Fig. 1.2.1). Hippocampus is developmentally older three-layered archicortex. Hippocampus proper consists of subfields of cells known as the Cornu Ammonis and the dentate gyrus. The Cornu Ammonis is subdivided into CA1, CA2 and CA3 subfields. Generally, rat hippocampus is divided into the ventral and dorsal part. Dorsal part is more engaged in processing of spatial information and learning and memory phenomena (Pothuizen et al. 2004) while ventral part is more employed in processes of emotion and behavioral inhibition (Segal et al. 2010).

In the transversal plane, principal hippocampal neurons are organized into so-called trisynaptic circuit (see Fig1.2.1). Neurons from layer II of the entorhinal cortex project via the perforant path to dentate gyrus and CA3 fields. Neurons in layer III of the entorhinal cortex project to the CA1 field of the hippocampus and to the subiculum via perforant and alvear pathways. The granule cells in dentate gyrus send their axons (mossy fibers) to the proximal dendrites of the



Human Rat

Trisynaptic circuit

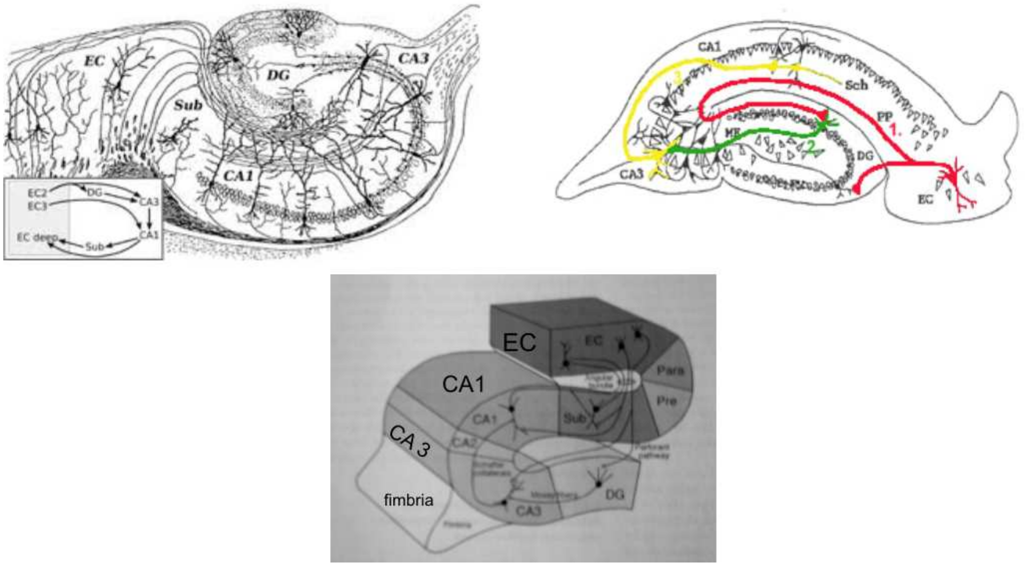


Figure 1.2.1: *A: Comparison of the human and rat hippocampal region (Source: left - adapted of Burgess et al., 1999; middle - adapted from source: http://www.ucl.ac.uk/jefferylab/research; right: adapted from source: http://synapses.clm.utexas.edu/anatomy/hippo/hippo.stm). B: Trisynaptic circuit. Left - human trisynaptic circuit was first described by Ramón y Cajal (original drawing from his book from 1911). Right: Sketch of the trisynaptic circuit in the rat hippocampus (source: http://www.ucl.ac.uk/jefferylab/research). Lower: Scheme of the trisynaptic circuit (adapted from The Hippocampus Book, 2007). EC - entrorhinal cortex, DG - dentate gyrus, Para - parasubiculum, Pre - presubiculum, Sub - subiculum. CA1-3 subfields of the cornu ammonis. Additional pictures were adapted from: http://synapses.clm.utexas.edu/anatomy/hippo/hippo.stm*

Structure	**Authors**
dentate gyrus	Jung et al. 1994
subiculum	Sharp and Green 1994
parasubiculum	Taube 1995
presubiculum	Sharp 1997
superficial and deep layers of the entorhinal cortex	Quirk et al. 1992, Frank et al. 2000

Table 1.2: *Structures containing place cells*

CA3-pyramidal cells. The CA3-pyramidal cells project to CA1-neurons via Schaffer collaterals. The CA1-pyramidal neurons project to the deep layers of the entorhinal cortex either directly or through the subiculum. The deep layers of entorhinal cortex, in turn, project to many cortical areas that originally projected to the entorhinal cortex. Therefore the information entering hippocampus via the entorhinal cortex traverses along the hippocampal circuit and returns back to the cortical areas where it originated. Most of the entorhinal input to hippocampus comes from the postrhinal and perirhinal cortices. The rhinal cortices receive input from all sensory modalities and from multimodal association areas and the hippocampus obtain multimodal and highly pre-processed information from neocortex in this way. From a simplified point of view, the hippocampal outputs are going through the entorhinal cortex and through the subiculum into subcortical regions (derived from Andersen et al. 2007, the Hippocampus Book, p. 108).

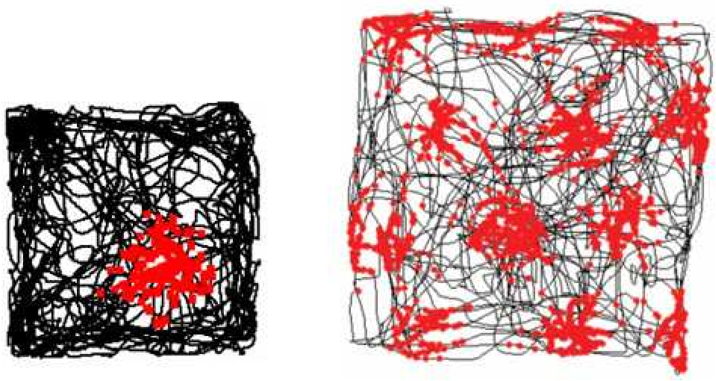
Place-specific activity of hippocampal neurons

O'Keefe and Dostrovsky discovered hippocampal neurons with subtle spatial specificity of their firing activity with respect to experimental environment (O'Keefe and Dostrovski 1971). These pyramidal neurons, called "place cells" were anatomically situated in CA1 and CA3 regions of the hippocampus (O'Keefe 1979). In consecutive studies, other subregions of the hippocampal formation containing place cells were discovered too (See Tab. 1.2).

Spectrum of place cell firing activity is changing during movement in space. When animal's head is located on a specific area, some place cell can increase its firing activity in a specific area, which is called firing field (See Fig. 1.2.2) (O'Keefe and Nadel,1978). In the classical open field arena, the specificity of firing fields is independent on directions by which animals approach them. However, when animal moves on a linear track, place cells are specific only in some direction of run. This phenomenon was shown in the linear maze (O'Keefe and Recce 1993) and in the radial-arm maze (McNaughton et al., 1983, O'Keefe and Recce, 1993). Frequency spectrum of the firing activity gradually increases from the periphery to the center of the firing field, but activity of one place cell is in general a highly variable phenomenon.

Place cells are controlled mostly by visual information from external landmarks, but this rule does not need to be absolute. When a salient external landmark is manipulated; e.g. by its rotation, place cell or ensemble of place cells usually rotated accordingly. Interestingly, when the same cue was removed, this failed to have any influence on the place cell activity (Fenton et al. 2000, a,b). This phenomenon traditionally pointed to the fact that information content of place cells is related to the space "as a whole" rather than to "particular fragments" of the space.

Representation of one environment by the place cells is built up during first minutes of exposure and exploration (Frank et al. 2004). Firing properties of place cells and their place specificity are different when animal is exposed to more than one environment, but this specificity becomes stable in each of the environments. Process, in which one ensemble of place cells (which is representing one environment) is "switched" (e.g. by means of translation of animal into another environment) into another ensemble of place cells, is called remapping. Each ensemble should be recalled again when animal entered environment once represented by one ensemble. Storing of such spatial information can last from hours to months (Muller et al. 1987, Thompson and Best 1990). Ensembles of place cells which represented in one environment behaved like a system with a high degree of plasticity. When one part of the environment was removed, it had no effect on place cell's representation of the environment. Ensemble of place cells "accepted" changes and still represented environment as a whole. Such capability of retrieving an entire representation from an incomplete input is called pattern completion. Generally, some authors attributed these properties to the massive recurrent



A place cell fires in one place in a square box

A grid cell (from Hafting et al) fires in evenly spaced peaks all over the box

Figure 1.2.2: *Right: Firing activity of a hippocampal place cell. Place-specific activity is plotted in red color. Left: Firing activity of a typical grid cell from the entorhinal cortex. Source: http://www.ucl.ac.uk/jefferylab/research*

collaterals in the CA3 and this led to hypothesis that hippocampus works as an “autoassociative” memory network (Marr 1971, McNaughton and Morris 1987, McNaughton and Nadel 1990, Treves and Rolls 1992, McClelland et al. 1995).

Place cells and salient distal and proximal landmarks

One of many questions of this thesis is about a difference between representation of distal and proximal landmarks, which are stable or moving. Despite the fact that several studies focused on landmark representation in space, most of the work targeted the visual brain areas. There are indeed many unanswered questions about the importance of the hippocampus for landmark representation. In this subsection I will mention some experiments, focusing on the place cells´ representation of salient distal and proximal landmarks.

Distal landmarks and firing of the place cells O’Keefe and Nadel’s cognitive map theory presupposed that distal landmarks are important for setting up the route, but not as suitable for specifying a precise location. This is because during an animal’s movement relations between landmarks do not change much (O’Keefe and Nadel, 1978). That is why distal landmarks are more suitable for “overall” navigation but local cues from apparatus and self-motion information are important for the more precise “tuning” of navigation. As mentioned above, when particular distal landmarks are removed, no change of the firing activity of most of the place cells is observed (O’Keefe and Conway, 1978; Muller and Kubie, 1987). Similar phenomenon was shown by the studies of Fenton et. al (2000 a,b) where majority of the place cells were associated to two salient cue cards inside a cylindrical arena. When one of the distal cues was removed and the remaining distal cue became rotated, a whole ensemble of place cells was still controlled by the remaining cue. This has shown an independent control by each card of each of a particular place field. We may ask if every place cell from a whole ensemble was bound at equal level or if place cells situated near the landmark displayed stronger control than place cell which was situated further away. The work of Fenton et al. (2000 a,b) answered this question unambiguously. When the angle between cards was changed, it influenced locations of place fields according to rotation of the displaced card. Firing fields of place cells which were closer to the card have been more affected than firing fields which were far away. Inherence of a particular landmarks or objects could be reflected by the increase activity of some pyramidal cells in the hippocampus. This type of neurons is so-called misplace cells. These cells are unique because reflect changes in the environment when a landmark or an object disappeared (O’Keefe 1976; Fyhn 2004).

Proximal landmarks and place cell activity Although distal landmarks can have fundamental influence on the firing activity of place cells, local and self-motion cues can also influence map-like firing activity of the place cell network in some cases. It was shown by recording place cells from blindfolded and deafened animals (Hill and Best, 1981; Save et al.,1998). These experiments showed that place cell activity are specific with respect to the idiothetic frame of reference; the place cell activity was bound to the shape of experimental set-up. Moreover, the study by Hill and Best (1981) showed that when rats were rapidly rotated together with the experimental arena for 20-30s with respect to distal cues inside the room, most of the place cells stayed controlled by local cues of the apparatus, while remaining place cells maintained their spatial selectivity with respect to the distal cues. This result pointed to the considerable link between perception of stimuli from rotating arena and place cell information. Other studies also demonstrated that proximal cues can affect the firing activity of place cells. The study of Gothard et al. (1996) examined the activity of place cells in rats running on the linear track between two places. The first place was a fixed site, while the second place was a movable box. Some of the place cells, as expected, specifically fired near the box with a fixed position, while other place cells fired in relative position to moved box. These data suggested that although map alignment can be controlled by landmarks, hippocampal neurons do not explicitly represent objects or events, and the proximal landmark on its own was not able to control place cell activity. However, under some circumstances, manipulation with distal vs. proximal cues revealed higher sensitivity or preference of place cell with respect to the proximal cues (Gothard et al. 1996).

1.2.2 Grid cells

These cells were discovered in the entorhinal cortex by Hafting et al. (2005). The entorhinal cortex receives signal from the head direction cells via presubiculum. It can therefore compare signal from heading of animal with signal about of metric of space represented by grid cells. These cells are characterized by grid-like specific firing activity in the environment (see Fig. 1.2.2). One function of the grid cells seems to be conveying information about distances in specific directions. “These cells maybe do not form the map of a given environment, but provide the Euclidean distance and direction metric postulated by the cognitive map theory of hippocampal function”(O’Keefe and Nadel 1978, Burgess et al. 2007). It was proposed that mutual interaction between grid cells, place cells and head direction system is fundamental for cognitive mapping (McNaughton et al. 2006).

1.2.3 Head direction system

Characteristics Head direction system is a system involved in processing of information for "spatial directions" (Taube et al. 1990, a,b). This system contains so-called head direction cells which are located diffusely in various limbic areas (Taube 2007). Firing activity of these neurons is specific for heading directional information in the space and is independent of actual location of the rat in the environment. Head direction system is also anatomically and functionally interconnected with the vestibular system and also with the hippocampal place cell and entorhinal grid-cell systems (Taube 2007).

This system for internal "compass" is represented by diffusely spread neurons with specific tuning for heading directions, so-called head direction cells. Head direction cells are neurons whose firing rate increases abruptly when animal's head is pointing to a particular direction (Taube 1990, a,b). Direction-specific firing activity might be plotted in x,y coordinates (Taube, 2007) or polar plot (Knierim et. al, 1995) (see Fig.1.2.3). Firing of neuron is specific for one direction in average directional range between 60 °~150°, in average value ~90° across neuron (Taube 2007). Firing activity of head direction neurons seems independent on the position of the animal in the environment and neither pitch or roll of the head within range ~90° of the horizontal plane . This activity is also independent of moving activity or actual behavior (Taube 2007).

Head direction cells were originally discovered by Ranck (1984) in the dorsal portion of the rat presubiculum (or also-called postsubiculum), but later were identified also in other limbic and extralimbic brain areas. These areas include anterior dorsal thalamic nucleus (Taube 1995), lateral mammillary nuclei (Stackman and Taube 1998), retrosplenial cortex (Chen et al.,1994), entorhinal cortex (Sargolini et al. 2006) and other non-Papez limbic structures, including lateral dorsal thalamus (Mizumori and Wiliams 1993), dorsal striatum (Wiener 1993), and medial precentral cortex (Mizumori et al. 2005), (for comprehensive review see Taube 2007). Head direction system is strongly coupled with vestibular system (Stackman and Taube 1997), system of hippocampal place cells, entorhinal grid cells (Caballero-Bleda and Witter 1993), and also with motor/proprioceptive system (e.g. Taube and Burton 1995). Each of the above-mentioned structures contains a different portion of head direction cells and all of these structures compose a complex network whose information flow through the postsubiculum and entorhinal cortex into the hippocampus, where both “directional” and “locale” systems are processed together (see Fig1.2.5).

Some authors suppose that head direction neurons are organized in virtual circle or continuous one-dimensional attractor network (Skaggs et al. 1995, Redish et al. 1996, Zhang 1996). This model, which was primary developed in computational modeling of activity of head direction system, presupposes interaction between interconnected neurons. Neurons with similar preferred direction excite recurrently and neurons with different preferred direction are inhibited and gradient of this activity composes “hills” or “valleys” which are changing according to actual heading direction of the animal (Taube 2007).

Head direction cells and distal *vs.* proximal landmarks Activity of head direction cells responds to visual distal landmarks. This is a well-known fact, confirmed by studies, in which manipulation of a salient cue, e.g. by its rotation, caused similar shift of head direction neurons (see also Fig.1.2.3, C) (Taube et al. 1990b). It is important to specify the character of the manipulation with a cue, which controls the head direction cells. In the first case when head direction neurons were clearly controlled by the cue manipulation, animals were taken away from the arena and disoriented while the cue on the arena was manipulated. Later, animals were returned to the arena. In another case when some cue was manipulated with animal on the arena, only salient cues were able to control the preferred direction of head direction cells, but “at the cost” of decreased accuracy (Taube et. al 1990b, Taube 2007). There also exists some similarity between experiments focused on the system of place cells and head direction cells; both with respect to salient landmarks. When some salient familiar landmark was removed, it did not have any influence on the activity of head direction cells (Taube et al. 1990b, Goodridge et al. 1998). Moreover, it also has been shown that salient proximal landmarks did not control the activity of

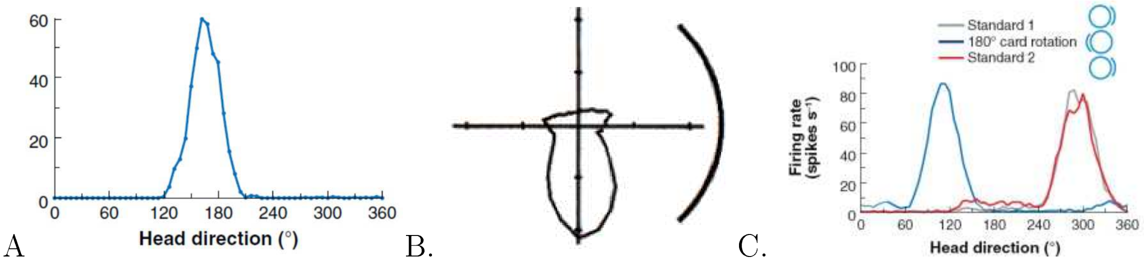


Figure 1.2.3: *A: Firing rate vs. head direction plot depicting various parameters used to characterize the firing properties of head direction cells - adapted from Taube (2007), Source: http://www.scholarpedia.org/article/Head_direction_cells. B: Polar plot of firing activity of a head direction cell. Adapted from Knierim et al., 1995 C: Responses of head direction cell from anterior dorsal thalamus following the 180°rotation.*

head direction neurons compared to background salient landmarks (Zugaro et al. 2001a). Multiple unit recordings have shown that head direction cells behave like an ensemble (or population) of neurons (Redish and Elga 1995). When one cue (from one specific direction) was manipulated, experimenters observed not only shift of a specific neuron with respect to a new position of the cue, but also shift of other cells in the ensemble. This interesting result pointed to idea that one salient cue is registered by whole ensemble of neurons (Taube 1990b). On this place it is worth to notice that the balance between the allothetic vs. idiothetic sources of information is provided to head direction system. Visual cue control of head direction system is not absolute. In some situations, e.g. when visual cues are brought into conflict with vestibular inputs, most of the head direction neurons tend to "utilize preferentially" the idiothetic source of information (Knierim 1998).

1.2.4 Posterior parietal cortex

Parietal cortex of the rat is defined as a posterior part of the cortex situated between the somatosensory and occipital parts of the cortex (Krieg 1946; Palomero-Gallagher & Zilles, 2004). Generally, this part of the brain seems to be involved in integration of multimodal sensory inputs (see Calton and Taube 2009). The parietal together with a retrosplenial cortex is functionally

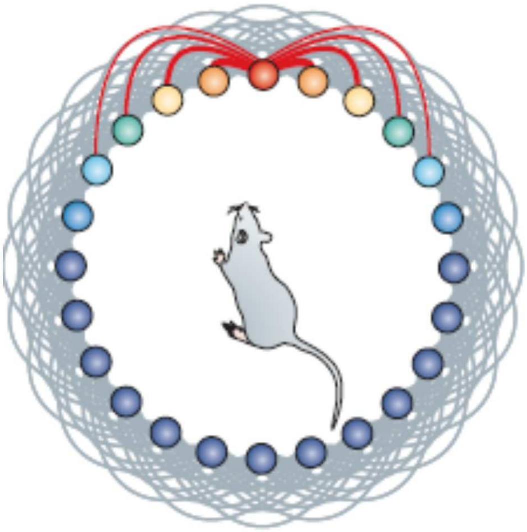


Figure 1.2.4: *Scheme of the attractor network of head direction cells. According to animal´s heading, only neurons which "cover" actual heading direction are active (referred as a activity hill) and remnant neurons from a "ring" remain inhibited. Adapted from McNaughton et al. (2007).*

interconnected with the temporal cortical areas and the hippocampus (Burwell & Amaral 1998a). These interconnections support the idea of involvement of the posterior cortical structures in processing or modulating spatial information from limbic structures. Some studies tried to compare the analogies between the rat and the primate parietal cortex. Similarity between the spatial neglect in primates and the rat model has been shown only in one study (King & Corwin 1993). One of the recent studies has focused on answering the question, which type of spatial information is relevant for posterior parietal cortex (Rogers and Kesner 2006). Results of this study pointed to double dissociation between hippocampus and posterior parietal cortex. Animals with hippocampal lesions were strongly affected in task, where allocentric type of information was important for task solution. Conversely, animals with lesions of the posterior parietal cortex were more affected in versions of task where egocentric type of information was important. A subsequent study by these authors has shown that posterior parietal cortex is important for manipulation with previously acquired information. It is noteworthy that rats which had lesion of the posterior parietal cortex were affected in manipulation of both egocentric and allothetic types of information. Interestingly

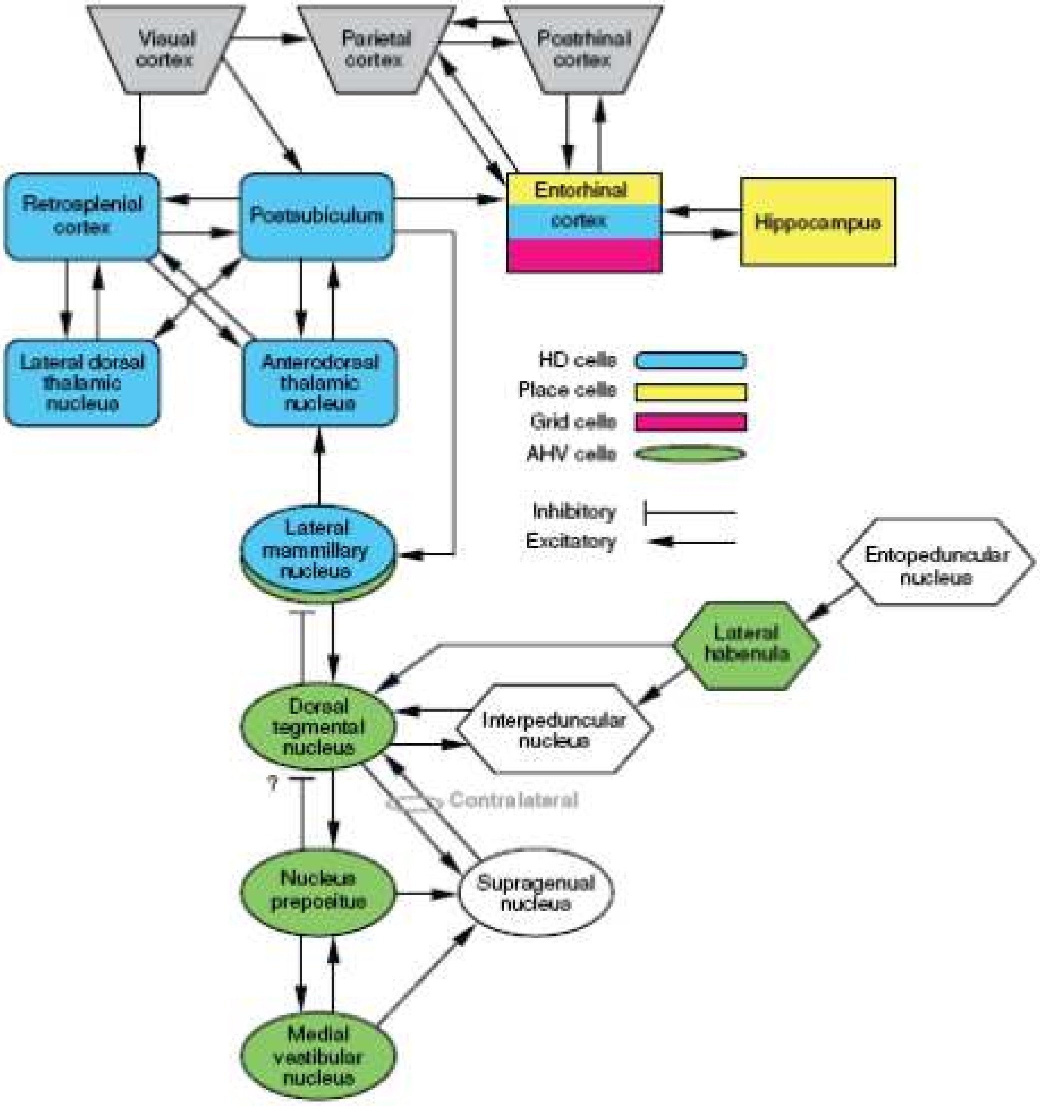


Figure 1.2.5: *Scheme of interconnection between head direction system containing head direction cells (HD), hippocampus containing place cells (PC), visual and vestibular system with angular head velocity cells (AHV). Adapted from Taube (2007)*

an electrophysiological study showed engagement of neurons from this region in manipulation with allothetic (auditory) cues (Nakamura 1999).

Chapter 2

Navigation in the moving world

In their everyday lives, people and animals actively navigate from place to place and interact with either a stable world or landmarks being in contemporary movement. Animals react to moving objects, e.g. to members of the same social group, mates, preys and predators. Similarly, human world is full of dynamic changes, historically starting with hunting of the prey, fighting, playing sport ball game or driving cars and flaying in the air-space. As for orientation in the stable environment, for a successful spatial navigation in moving world, it is necessary to collect processing of many variables, e.g. determining and recognizing places, estimating distances and various directions and vectors between moving world and a subject. Environment could be perceived as “dynamic” or “moving” in two basic situations: In the first one, the world chnages as a whole, e.g. when we are actively or passively translated. In the second one, only part of the environment moves, e.g. there is an active movement of a target (prey, ball, member of the social group) or target may relatively approach the subjects; when an obstacle subject is prsent and changes its relative position.

In this chapter, I will first outline the rationale presupposed for studying principles of navigation in dynamically changing environments. I will also focus on a problem, how animals organize their behavior, memories and neural activity when organizing the world into so-called multiple reference frames. For perceiving changes in the moving world "as a whole", it appears important to have visual inputs about actual positions of landmarks or dynamics of optic flow, but it might not be absolutely substantial and final source of information. In the second part of this chapter will be introduced an overview of importance of so-called inertial inputs (which are based mainly on vestibular, tactile and proprioceptive inputs) for spatial cognition in stable and dynamic world. Third section of the chapter will be focused on the processing of the information about moving landmarks in various animal species and also in the rat. I will introduce some strategies of approach and also avoidance behavior and the end of this section will introduce some experimental findings about neural basis of a processing information about particular moving objects.

2.0.5 Space and its organization and segregation of spatial stimuli

Manipulation with cues

Spatial navigation can be accomplished by using several navigational strategies and each strategy requires appropriate computations and specific types of information (Fenton and Bures 2003). Example of such situations could be seen, when considering animal searching for a hidden goal. Although the goal is not directly perceptible, hidden place can be defined by mutual spatial relationships between particular positions of distal oriented cues (e.g. allothetic information). This process requires organizing and storing this information into a representation, which can be used for finding the directly imperceptible goal. Another representation of the same environment is also conceivable. The above-mentioned praxis or path integration represent alternative strategies, which does not depend on external inputs, but it is also possible to use different representation based on a set of proximal cues on the arena and an information from a self-motion (e.g. idiothetic information). Experimentally, it is possible to dissociate allothetic representation from idiothetic representation e.g. in the Morris water maze task. For a successful finding of a hidden platform, only a set of exteroceptive stimuli is relevant, while idiothetic information is limited and not useful.

Moreover, it is also possible to experimentally dissociate idiothetic and allothetic representations. Some behavioral tasks on a dry arena allow removing exteroceptive cues by simple switching-off the light (in detail described bellow in a homing task).

"One off" rotating arena Experimental group of Jan Bures developed a broad set of behavioral tasks, which are important tools for studying basic mechanisms of dynamic organization of the spatial information from behavioral as well as neural point of view. When an animal solves spatial task on a stable arena, one usually cannot distinguish which source of spatial information animal actually operates, e.g. it is not possible to determine which set of cues the animal uses for navigation. In one of the first experiments from a long series, Bures, Fenton and their colleagues developed so-called place avoidance task, in which rats had to avoid a triangular sector of the circular arena. Animals foraged for randomly scattered food and simultaneously avoided the forbidden sector. When animals entered the to-be-avoided sector, they obtained mild foot shock. Animals were trained until they reached the criterion. The room was then made completely dark and the shock was disconnected. Surprisingly, the avoidance of the to-be-avoided sector continued longer than 30min. After one training session the rat was removed from the arena and light in the room was switched on again and the arena with cues was rotated by an angle of 180 ° from its original position. The idea was to return the animal back to the arena where arena cues were changed but animal internal sense of position would be unaffected. The authors had expected avoidance only of the position of the sector defined by the external visible cues. Moreover, animals surprisingly were correct in avoidance of both two positions defined by external room-bound cues and also by arena-bound cues.

Carousel arena Paradigms described above had contributed to the method using continuous rotation of the arena (see Fig.2.0.4), (Bures 1996, Moghaddam and Bures 1996). External cues outside the arena, i.e. room-bound cues (RBC), are continuously dissociated from the idiothetic information and proximal cues on the arena, i.e. arena-bound cues (ABC). This method was designed for testing hypothesis if memory from RBC and ABC could be acquired separately and how this memory can by expressed or extinguished by manipulating either available ABC or RBC (Bures et. al., 1997a, 1998).

Figures 2.0.1-8. summarizes a series of experiments manipulating with ABC or RBC. As tools for controlling the available sensory information, rotation or stopping the arena together with darkening or illuminating an experimental room were used. In general, when the arena was continuously rotated, ABC were still perceivable, but dissociated from RBC. Darkening the room removed RBC, while the arena-bound information still remained available.

Rats were at first trained in an acquisition phase (AP) in light. When their performance reached asymptotic level, (i.e., an avoidance criterion), lights and shocks were switched off and next part of the experiment started - extinction phase I. (EP1) This session continued until the criterion for extinction was reached. When avoidance of the sector in the EP1 phase was extinguished, lights were switched-on and the test continued again, until the criterion for the extinction was reached - extinction phase II (EP2). Experiments were designed so that during the AP, the arena was either rotating or stable. Similarly, during both extinction phases the arena was either rotating or stable, but for both phases together.

The main result of this experiment was the finding that memory defined with respect to one of the ABC or RBC depended on the training protocol and availability of the cues. When the arena was stable in AP, both ABC and RBC overlapped and animals acquired representation of the position of the to-be-avoided sector defined by both ABC or RBC. When the arena in EP1 and EP2 was still stable, avoidance for both ABC and RBC defined sector were “definitely” extinguished for both ABC and RBC. On the other side, when the arena remained rotating in EP1 and EP2, only avoidance for ABC defined sector was “definitely” extinguished but avoidance for RBC in EP2 remained stable for a long time.

When the arena rotated in AP, only the sector defined by RBC was acquired, and this manifested as slow extinction in both EP1 and EP2 (see Fig. 2.0.3 and 2.0.2). Representation defined by

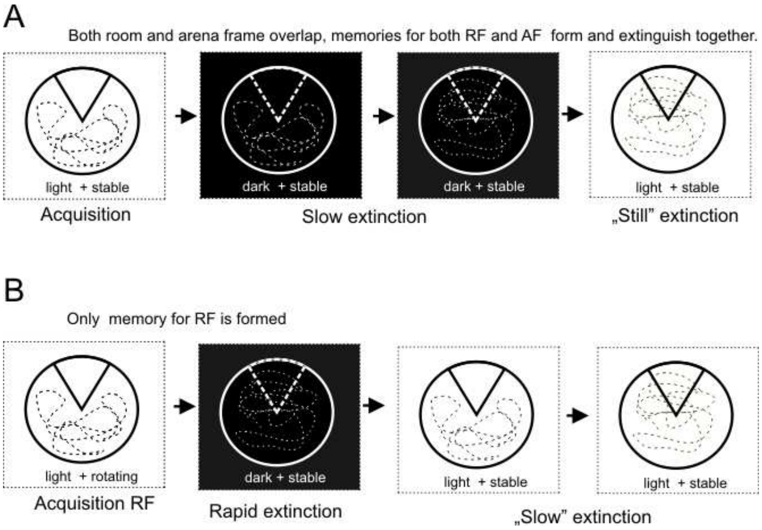


Figure 2.0.1: *Scheme of experiments, based on Bures et al., (1997a) and Fenton and Bures (2003).* **A**: *Acquisition phase: rats were trained on a stable arena. Extinction phase I.: External stimuli were removed and animals avoided to-be-avoided sector for longer than 30min. Extinction phase II: Room was illuminated again and animals still did not remember the position of the sector, because the extinction for both frames had completely finished.* **B**: *Acquisition phase: Rats were trained on a rotating arena and only memory for a room frame has formed. Extinction phase I. Immediate extinction occurred, because external stimuli were removed in darkness. Extinction phase II: After swithing on the light, memory for the room-frame-defined denied sector persisted for long a time.*

ARC was not available, because during the rotation the shock reinforcement could be delivered in any place of the arena.

The above described experiments show that animals necessarily operate with two sets of spatial stimuli. When the arena was stable, both sets of stimuli overlapped and composed unique so-called stable reference frame (RefF). When the arena rotated, RBC were dissociated from the ABC, and ABC “still” remained stable RefF and RBC “became” “rotating” RefF. Generally, RefF is a space in which animals organize their behavior. Experiment of Fenton et al. (1998) showed that rats naturally organized their behavior into different RefFs (see Fig.2.0.4 and 2.0.5). In this experiment, which followed the above described experimental series, the animals were trained again to avoid a shock sector on the stable arena. When the rats were overtrained, the shock was turned off and both ABC, or “arena frame” (AF) and RBC or “room frame” (RF) were dissociated by rotating arena. Now, the rats still avoided both AF and RF defined sectors showing that they used both

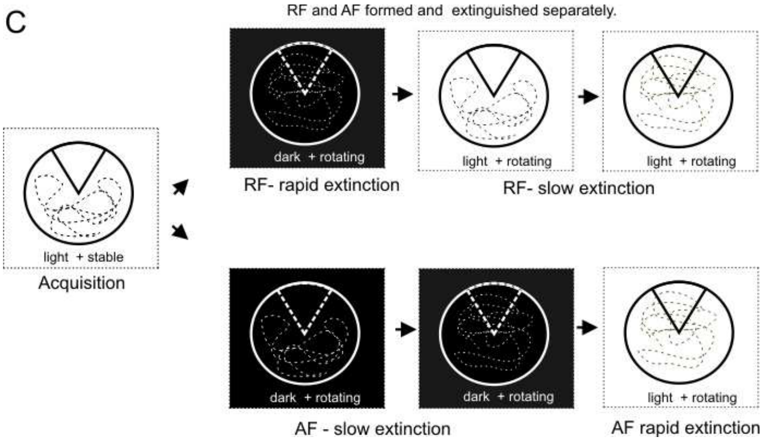


Figure 2.0.2: *Scheme of experiments of Bures et al. (1997a) and Fenton and Bures (2003).* ***C****:Acquisition phase: Rats were trained on the stable arena. Extinction phase I.: External stimuli were removed and animals did not avoid the to-be-avoided sector defined by the room frame. The to-be avoided sector defined by arena frame was avoided at least for 30min. Extinction phase II: Room-defined sector was available for navigation. Arena-defined sector was extinguished.*

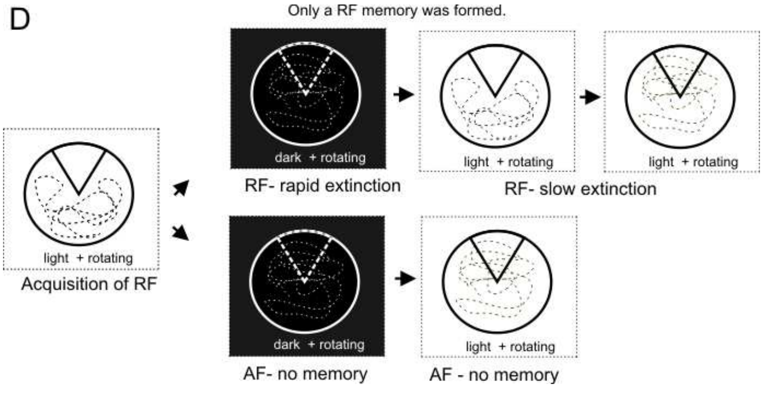


Figure 2.0.3: *Scheme of experiments of Bures et al. (1997a) and Fenton and Bures (2003).* **D***: Acquisition phase: Rats were trained on the rotating arena. External stimuli were removed and animals did not avoid the sector defined by room frame. The sector defined by arena frame was not acquired. Extinction phase II: Room-defined sector was available for navigation.The sector defined by arena, however, was not.*

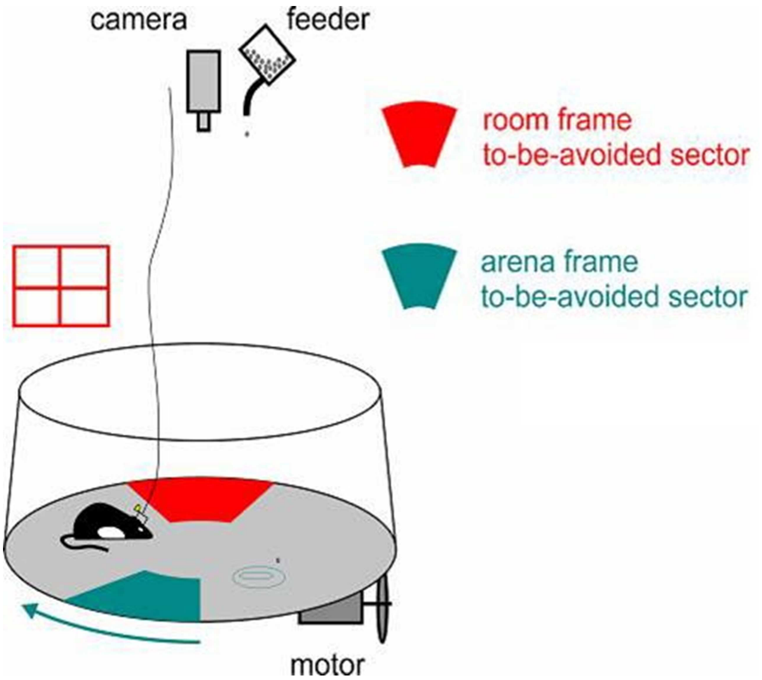


Figure 2.0.4: *Scheme of* ***the Carousel Arena****. In this version, animals avoided two sectors, which are dissociable by arena rotation. Red sector is defined by the room frame, position of the green sector is defined by arena-bound cues.* ©***Daniel Klement***

RefFs simultaneously.

Hippocampus and reference frames

Organization of spatial information As described above, neural correlates of spatial information in stable environments are relatively well-known but these studies do not reach more subtle interactions between potential neural subgroups coding mentioned multiple RefF in non-stationary environments. Some experiments (Zinyuk et.al 2000, Kelemen et al. 2010) used recording of place cells activity on the rotating arena to evaluate if these neurons are also organized with respect to particular RefFs.

Generally, place cells on a stable arena became disorganized and silent after starting the rotation of the arena, some place cells were bound to one of the perceiving RefF and some of them were specific for both RefF (Zinyuk et. al 2000, Kelemen et al.,2010). Notably, the proportion of mentioned

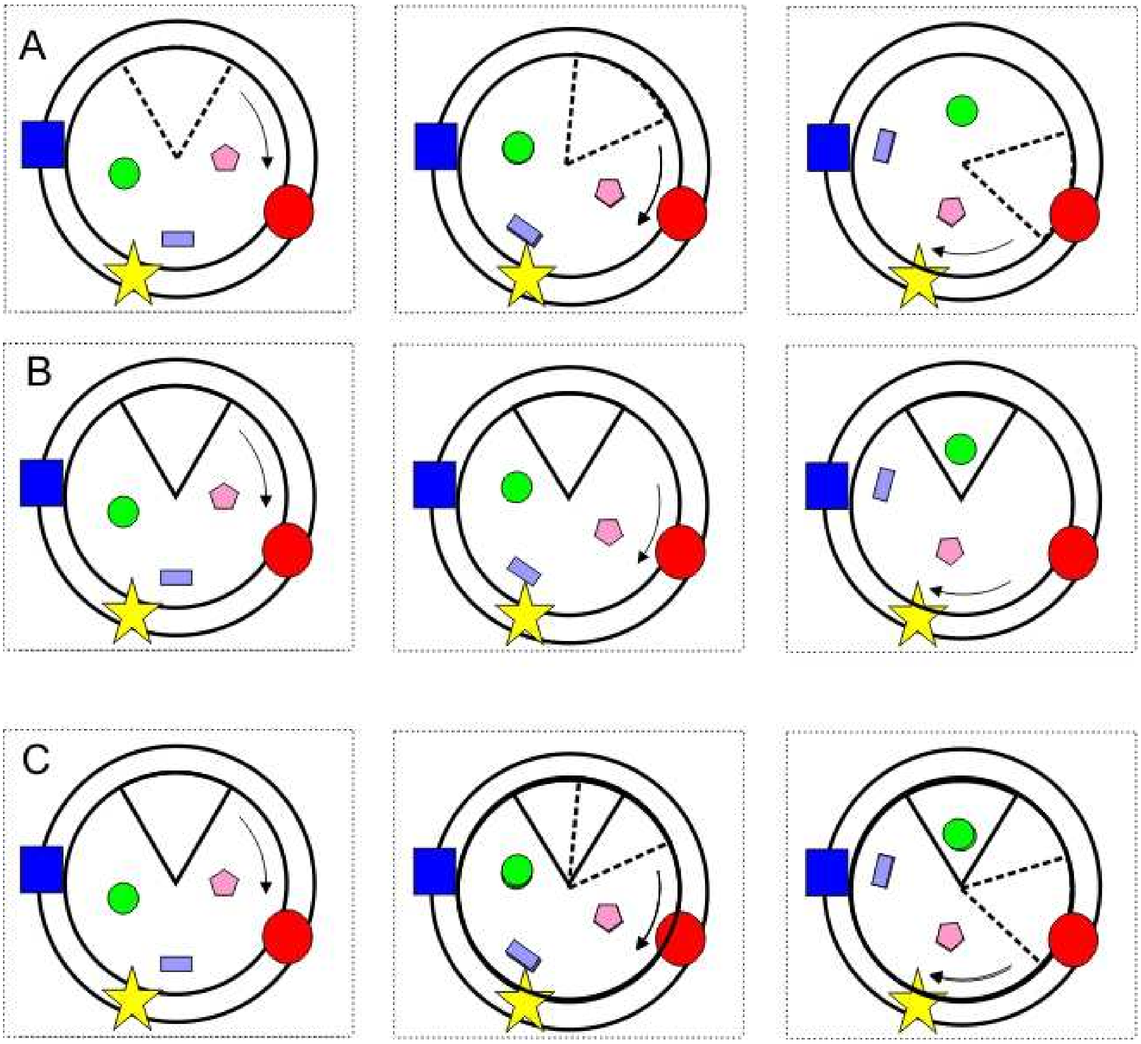


Figure 2.0.5: *Principle of a distribution of 60° sector in the Carousel arena. Configuration of the triangular-like sector (which could be extended to the center of arena or truncated). Animals were trained to avoid the sectors in various paradigms. A: Avoidance of the arena-defined sectror. B: Avoidance of the room-defined sector (it is the most frequently used version of the task, often called "**a**ctive **a**llothetic **p**lace **a**voidance (AAPA task). C: Avoidance of two sectors defined by both arena and room-defined cues. This version of the task is also called double place avoidance task.*

subgroups of place cells depended on the behavioral context of the testing task. Zinyuk et. al (2000) recorded place cells in rats running on stable and rotating arenas. Animals were divided into two subgroups. first group was foragers, which experimental environment "only" randomly searched pellets of a food on the arena. Second group was navigators, which were trained to navigate in the arena in a place preference task (Rossier et al. 2000). When animals became familiar with the environment, arena rotation has started. Most of the "familiar" place cells in foragers loss their spatial specificity, but in navigators firing of their place cells remained mostly stable with respect to the environment. These neurons were either AF - or RF-specific; only small proportion was specific for both RefFs or lost their spatial specificity. This result indicates that navigators were more familiar with the space, because they used it for solving the navigational task and the place cells were more anchored to particular reference frames (Zinyuk 2000). Previous studies also showed that place cells could organize themselves into various types of neurons coding various types of RefF (see also Table 2.1).

Results mentioned above give rise to a question about possible role of hippocampus in organization of the information about reference frames. Is the hippocampus only a "storage site" of spatial memory sorted into the RefFs or does some "higher level of process" exist there? To evaluate this question Cimadevilla et al. (2000, 2000 a, b, c, 2001b) developed a new version of place avoidance task (see Fig 2.0.5). Rat or mouse were placing on the carousel arena and had to actively avoid a forbidden shock sector defined with respect to RF or allothetic set of cues respectively. Active avoidance of allothetically defined denied sector set the name of the task - Active allothetic place avoidance task (AAPA). This task requires organization of the spatial information with respect to the two dissociated RefFs. For effective identification of shock place animals had to associate the sector with RBC and simultaneously inhibit the ABC. Beside "knowledge" about itself position of the denied sector, next precondition is knowledge of its own position inside the RF.

Authors	**Reference frames and place cells**
Zinyuk (2000)	In rat "navigators", neurons specific for two reference frames dissociated by arena rotation were found. In rats which only "foraged", similar division was not observed.
Gothard et.al (1996)	During behavioral task, 5 reference-frame groups of the place cells were found which were specific for particular "relative" position during solution of the task despite the fact that the "absolute" position of the animal had changed.
Jeffery et al. (1997)	Firing of place cells was found to be sensitive for RefF defined by internal sense of position as well as by physical appereance of the environment.
Wood et al. (2000)	Different place cells represented different parts of the modified T - maze. Some of the place cells overlapped.
Redish et al(2000)	Place cells were recorded on a linear maze with a box, the position of which was changed. Some place cells were defined by "box frame", others by "trajectory" in maze.
Kelemen et al. (2010)	Two groups of place cells represented two frames dissociated by arena rotation, which had to be avoided simultaneously. One group of neurons was specific for one reference frame, whilst the second group of neurons was specific for both frames.

Table 2.1: ***Examples of studies showing representations of various reference frames by place cells.***

Segregation of information Traditionally, hippocampus is thought to encode spatial representation in an associative network, postulated by distributed memory hypothesis (McNaughton and Morris, 1987; for review, see Lisman, 1999). Memory for spatial representation is hippocampus dependent, and in both processes of acquisition or retrieval it is employed different amount or distributed subset of connections encodes memory in a hippocampal tissue. This declared experiments in which lesion of one hippocampus does not influence acquisition, but abolish retrieval of the memory in water maze task (Moser et al., 1993, Fenton et al., 1993). Surprisingly, the different pattern were observed, when the same protocol was used in an acquisition or retrieval phase when testing the AAPA task (Cimadevilla et.al, 2001c). In this study the ability of avoidance was abolished in every phase after the unilateral inactivation. The fact that memory for AAPA task is abolished after the unilateral hippocampal inactivation is in accordance with mentioned distributed memory hypotheses, but this point of view is not so clear. This account failed to explain why the same injections of TTX injected into the hippocampus spared learning and retention when room and arena stimuli were not dissociated by rotation of the arena, but abolished the avoidance of the same sector when the two frames were dissociated by rotation (Wesierska et al. 2005, Kubik and Fenton 2005).

On a basis of these studies, the authors Kubik and Fenton (2005) tested the hypothesis that in hippocampus representational memory and process of stimulus segregation are distributed like two independent hippocampal functions. The authors confirmed predictions that the amount of hippocampal tissue with distributed hippocampal network participating in processes of spatial segregation would depend on the phase of the learning process. The authors in accordance to previous studies predicted that AAPA task is "more" burdened by process of segregation spatial stimuli than their representations of the relation between the stimuli, because to determinate the position of the "large" sector is not too "difficult" for spatial computation than mentioned water maze task, which is based "more" representationaly . Segregation of relevant and irrelevant stimuli is the first step for a successful solution of this dynamic task. When the relevant stimuli are com-

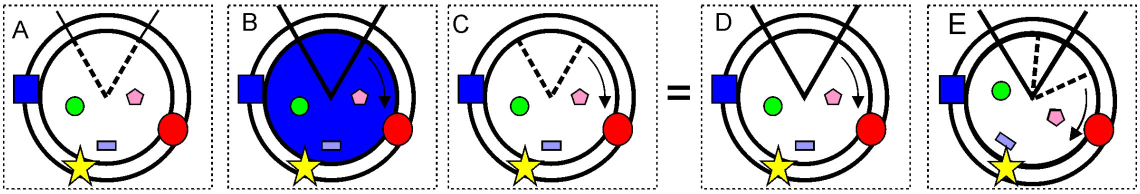


Figure 2.0.6: *Hypothetical scale of "degree" of the segregation processes in the place avoidance task. Segregation demands increase from A to D. A: AF and RF overlap, no demand for segregation is required. B: The arena rotates and animals avoid RF-defined shock sector. Shallow water masks arena and olfactory cues and rotation dissociates self-motion stimuli. C: Arena rotates and animals avoid RF-defined sector. This protocol has greater demands for segregation, because animals must dissociate olfactory stimuli and stimuli from the arena. D: Hypothetically higher or equal segregational demands in the situation, when animals avoid AF-defined sector. This procces also requires dissociation of inertial stimuli deived from passive movement, from the self-motion stimuli perceived during active movement. E: The highest level of segregational demands in the double place avoidance task. Animals must avoid two sectors defined by both AF and RF.*

promised, acquiring the association between relevant stimuli and/or responses will be retarded by interference from irrelevant associations. Once the appropriate associations are formed, segregation is less critical in subsequent phases, because only the relevant stimuli will have strengthened associations to appropriate responses (Kubik and Fenton 2005). In accordance to these predictions, the partial lesion would not influence the retrieval of the acquired memory in AAPA, but failed the process of acquisition of learning process. The authors also supposed the idea about the "scale" for segregation process of the stimuli in the AAPA task based on various amount of removing or vice versa adding different modality of sensory inputs which had to be segregated like a relevant or irrelevant stimuli. For an optimal "tuning" of the experimental task the authors arranged the task by decreasing a degree of segregation process. They arranged AAPA task (see Fig. 2.0.6) by putting shallow water which hidden stimuli on the arena. Such decrease of the "segregation level" would hypothetically enable to use 50 % of the hippocampal tissue for retrieval of stimulus segregation process.

2.0.6 Inertial inputs and spatial cognition

Perception of changes coming from the active and passive body movements is a prerequisite for spatial cognition and memory. In this section I will summarize current knowledge about the importance of inertial stimuli in spatial cognition.

Definition of “inertial” forces

Animals and human and some machines may process information about changes of their body in the space during their active movement. These sources of information are also called inertial stimuli. In technical literature, some basic sensors for inertial navigation are described. An example could be sensors for linear motion (accelerometers), rotations (gyroscopes), or velocity (direction and movements). These navigation systems work without the need of external sources of information (http://en.wikipedia.org/wiki/Inertial_navigation_system). Definition of the “inertia” comes from the Latin word, "inners", meaning idle, or lazy (http://en.wikipedia.org/wiki/Inertia). Inertia means resistance of any physical object to a change in its state of motion or rest. It is represented by mass of object. The principle of inertia is one of the basic principles of classical physics which is used to describe the motion of matter and how this is affected by the external forces. Sir Isaac Newton defined inertia in definitions 1 - 3 of his Philosophiæ Naturalis Principia Mathematica (1846) (http://en.wikipedia.org/wiki/Inertia). Inertial environment is environment which is in quiet state. Non-inertial environment is affected by the external forces applying movement of this environment. An example of a non-inertial environment is passive movement in the carousel arena or in the moving car. If the subject situated inside the non-inertial environment (e.g. sitting on the carousel) is in a relatively quiet state, he can still perceive accelerations and decelerations from the passive movement. Linear translation or rotation produces linear or centrifugal accelerations. Both accelerations directly mediate perceiving of changes in vestibular system, skin mechanoceptors or proprioceptors. Stimuli invoked by such inertial forces we call “inertial stimuli”. Next part of this section will be focused mainly on the role of vestibular component of inertial inputs. These inputs seem to have a most considerable role for spatial orientation and memory.

Dead reckoning (DR) As we have seen above, animals usually control its own position by using a distal allothetic cues during exploration of the space by means of so-called pilot exploratory behavior (PEB). Sometimes the source of allothetic information is not available for some reasons (e.g. in novel environment or when the landmarks in familiar environment are either absent or in conflict with previous experience) (Wallace et al. 2008). At these times animals can utilize alternative sources of spatial information arising from the animal´s active or also passive movement. Besides efferent copies of motor commands or sensory flow (see Fig. 2.0.7), the other sensory sources are available. Accelerations and decelerations are sensed by the vestibular system, proprioceptors and skin mechanoceptors. This is used for directional information from changes of animal heading and is generally used for location of the subject's actual position or with respect to starting position e.g. the beginning of the exploratory trip or home nest. This form of navigation, e.g., when animal returns back to a home nest by using path integration, is called dead reckoning (DR)(Gallistel 1990). The first who described this form of navigation in wildlife was Charles Darwin (Darwin 1873). Under natural conditions animals must obtain food from the environment while avoiding predation. This behavioral paradigm was described in many laboratory experiments (Mittelstaedt and Mittelstaedt 1980, 1982, Etienne 1980). The most interesting phenomenon is that after an exploratory trip (animals navigate by PEB), a very quick return into the home nest by direct way follows (animals navigate by DR). Direct return way can pass through the places which animals had never visited. The most compelling phenomenon in DR is that it "works" even when all allothetic cues are removed (e.g. by simple switching off the light). Several authors (e.g. Whishaw 2001, Etienne 1980) studied the importance of particular idiothetic inputs in DR. The most critical problem was dissociating vestibular and proprioceptive sensory inputs. Older experiment with golden hamsters studied influence of the passive transportation in the outward trip in DR. This study had shown that animals used only information about angular but not about

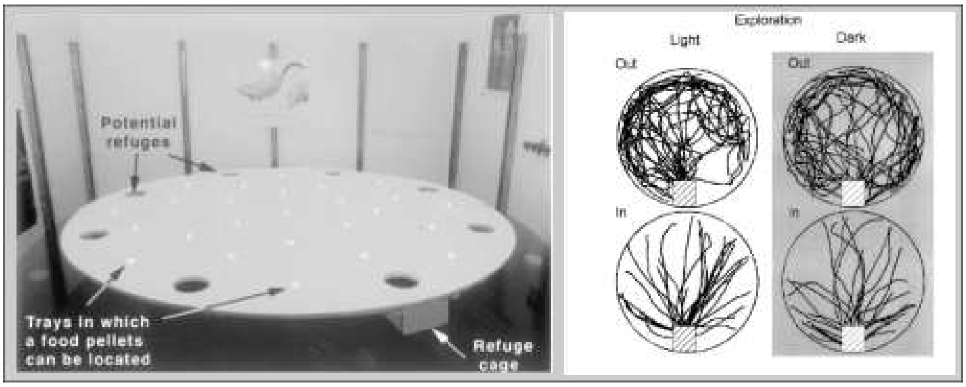


Figure 2.0.7: Patterns of outward (out) and homeward (in) trips in the light (left) and in the dark (right). Each panel shows five trips by each of the six rats. Note that the outward trips were circuitous, whereas homeward trips were direct, adapted from Whishaw et al. (2001).

linear accelerations to derive consecutive homeward trip. Earlier study done by Séguinot et al. (1998) showed that animals used both angular and also linear acceleration during outward trip for deriving homeward trip. Importance of the vestibular system for DR also has been also shown by consequent experiments. Whishaw et al. (1995, 1996, 2001) trained rats to find pellets of food on a large circular arena with the home base located on the periphery above or under the arena (probe test). When the rat found a piece of the food than it returned back to the home nest. Trajectories of animals were fragmented into PEB and DR on the basis of the changes of the speed profile of the animal's movement (see Fig. 2.0.7). Wallace et al. (2002) tested DR in labyrinthectomized rats. They found no influence of the lesion to the homeward trip in light with respect to both visible or hidden home nest, but a strong affection of the homeward trip in the darkness (Wallace 2002). These rats were also tested in a discrimination cue control task, when a new refuge position was presented. When both groups of rats found the pellet, they have first returned at the former place, but only control rats have consequently returned to the new place. Vestibular-lesioned rats moved around the arena and evaluated the former position several times. This result indicates that rats with vestibular lesions rely more on environmental cues than self-motion cues and this finding is consistent with other work (e.g. Stackman and Herbert 2002).

View-centered representations Perception of the inertial stimuli (mainly vestibular stimuli) applied during locomotion can exert an important influence not only in a "classical" process of path integration, but also in updating of view-scene recognition. Despite this type of navigation appears to be a visual strategy, in some cases perceived vestibular inputs seem to be crucial. This was illustrated by several experiments with humans when subjects were required to recognize some locations from their view-centered position in space during an active locomotion or even without active movement. In one experiment, children were shown a toy being hidden. Children were then either carried to a place on the opposite side of the experimental room or they were allowed to move themselves to a new place. When children have subsequently searched the toy, children who actively moved were more successful rather than children who passively observed the position of the toy (Benzon and Uzgiris 1985). Subsequent studies have also compared active movement in space with its passive viewing and confirmed the advantage of the active exploration over passive observing (Poag et. al 1983, Benson and Uzgiris 1985). People, who observe actively, are also able to estimate future positions better or even to generalize to novel views of the same scenes and navigate through the space (Larish and Andersen 1995, Christou and Bülthoff 1999). In a follow-up study, Simons and Wang (1999) have studied view-centered representation of scene after either a passive rotation or active walk around a circular table with objects. Subjects viewed the objects on the table and than were asked to detect an object in array that had been moved. When the table (and view of the object array) rotated, performance of subjects was worse than in situation, when subjects actively moved and table remained stable (but subjects saw a new view of the scene). The same results were also obtained when subject actively rotated the table himself. Here, subjects were better at the previously studied position when tested from this position, but were better at the rotated view when they were tested at the new position. These results suggest that subjects updated their egocentric based representation of the object array during active locomotion. Process of updating egocentric representation was disrupted by disorientation between the initial observation and the test.

Vestibular system and memory

There exist several points of view on vestibular system (VS) and its connection with memory mechanisms. Here, we will evaluate only two views. First point of view deals with a relationship between the VS and limbic structures containing hippocampus, the structure fundamental for spatial learning and memory. Second point of view is about "memorization process" for motion in space. An example could be a memory of movement sequence arising from optic flow or from series of vestibular stimuli during self-motion. This dynamic, spatiotemporal process is based on perception of multimodal signals, including mainly visual, vestibular and proprioceptive inputs.

Memory for space Strikingly, it has been shown that information from the vestibular inner ear participates in the spatial learning and memory. This is evident from behavioral experiments (Beritoff 1965; Potegal et al 1985, Etienne 1980, Semenov and Bures 1989, Israel et al. 1996, Zheng et al. 2003, Etienne and Jeffery, 2004; Kirwan et al. 2008), as well as from experiments with vestibular lesions (Chapuis et al 1992; Zheng et. al 2006, 2007, 2008), or from experiments in human (Loomis et al, 1999). There also exist several studies reporting relationship between VS and other types of memory (Schautzer et al., 2003, Brand et al. 2005) or the other cognitive abilities (Risey and Briner, 1990, Zheng et al., 2004).
Lesion studies in animals (see Table 2.2) showed strong alterations of the spatial learning after selective vestibular ablations. It should be noted that spatial memory was altered more after bilateral than unilateral lesions of VS and effect of a cognitive impairment was not due to an inability to move, because the animals often exhibited locomotor hyperactivity then hypoactivity compared to controls. Cognitive deficits have been ameliorated with time, but performance of animals with lesions of VS was significantly worse than of control animals.

Memory for movement VS seems to be important for remembering of a sequence of the self-motion events. This is obvious from a set of experiments which showed that subjects are able to

Method	Author	Main result
Morris water maze	Petrosiny (1984)	„Hemilabyrinthectomized animals showed impaired swimming behavior, which has improved over time (within 21–25 days)”
	Stackman and Herbert (2002)	Rats required visual landmarks for estimating position of the hidden platform.
Radial arm maze	Herr et al.(1989)	Bilateral labyrinthectomy produced a profound decrement in performance to find rewarded place, when animals had to use only vestibular inputs.
	Chapuis et.al (1992)	Inability of subjectsto maintain a correct angular trajectory.
	Ossenkopp and Hargreaves (1993)	Lesioned rats made significantly more sequential same arm reentries and fewer sequential adjacent arm entries than controls.
	Russel et. al (2003)	Rats exhiited long-term changes in performance in spatial reference memory task
T- maze	Zheng et al.(2007)	Long-term deficit in spatial forced alternation in a T-maze after the BV lesion but with recovery of function.
Foraging task	Walace et. al. (2002)	Inability to return into the refuge in the dark and also to new position of the refuge in the light.
	Zheng (2006)	Rats with unilateral lesions of the VS were disrupted in dead reconing at least for three months, while rats with bilateral lesions were affected at least for six months.

Table 2.2: *Overview of selected behavioral experiments on spatial learning and memory in animals with lesions of vestibular system.*

reproduce passive displacements in darkness. For a successful solution of this task, a person is required to reproduce distance or velocity profile. Berthoz et al. (1995) investigated blindfolded subjects in such test, sitting on the movable and joystick-controlled chair. Participants were able to reproduce both speed profile and distance from the passively acquired movement with a high accuracy, which implies that all spatiotemporal properties of movement can be stored in the brain. This is based on the dynamic reproduction of memory and actual incoming information based mainly on the vestibular and kinesthetic cues. Accuracy of spatial memory in environments with decreased perception of locomotion also depends on currently available, albeit limited sources of information from VS or optic flow (Redlick et al. 2001; Harris 2000). Another appealing question is how memory for the movement is stored in such situations, when multiple sensory cues are available. It can be hypothesized that there exists only one common memory which may be composed from all sensoryinputs or alternatively, each sensory input have its own memory storage site or a buffer. Vidal et al. (2010) studied process of memorization of vestibular inputs and optic flow during passively induced upright turns. Experimental setup allowed for precise control of passively induced movement by using either vestibular or optic flow stimuli presented independently or together. Participants had to reproduce movement on the joystick-controlled chair in three experimental protocols. In first two experiments, subjects had to reproduce upright turns when only unimodal source of information was available. In the third experiment, subjects had to reproduce upright movement when bimodal information was presented. Performance of subjects was similar in both cases when only vestibular or optic flow stimuli were present. In cases when both types of stimuli were available, such bimodal reproduction was more precise and its variance laid between the two unimodal reproductions.

Vestibular system and the spatial brain

Functional connections There exists a number of experiments indicative of interconnections between the hippocampus and vestibular system. Anatomical, neurochemical (Horii et al.,1995) or electrophysiological (Horii, 1994) evidence showed that inputs from the svestibular system affect hippocampal formation or HDS. Electrical stimulation of vestibular labyrinth (VL) (Horii, 1994, Cuthbert et al, 2000) or its bilateral removal in rats (Russell et al., 2001, 2002) significantly affected signals generated in the hippocampus. Electrical stimulation of VL and electrical signals incoming to the hippocampus evoked potentials which traveled in rostro-caudal direction across CA1, and elicited theta activity in both anesthetized and awake guinea pigs Cuthbert et al. (2000). In addition, Cuthbert et al. (2000) described in guinea pigs that inputs coming from peripheral vestibular system after its stimulation evoke electrical activity in the hippocampus arriving there with latency of approximately 40ms. There are also studies in humans supporting results of animal studies. For example, in people after an unilateral caloric stimulation of the vestibular system, ipsilateral activity in the hippocampus was increased together with other cortices, e.g. posterior insular cortex, BA 7, retrosplenial cortex and subiculum (Vitte et al.,1996). In spite of a strong cooperation between the vestibular system and hippocampal complex, there is no direct connection between these structures (Smith, 1997; Cuthbert et al., 2000; Horii et al., 2004). Vestibular nucleus complex receive mainly monosynaptic inputs from the ipsilateral vestibular nerve and project disynaptically mainly to the parietal and visual cortices. It is assumed that connection of VS with the limbic structures is polysynaptic and can be conveyed along three ways (see Fig. 2.0.8).

"Inertia" and place cell activity A great deal of evidence about the cooperation between hippocampal neuronal network and vestibular system was demonstrated in experiments using single unit recording. O'Mara et al. (1994) found that hippocampal neurons of monkey were modulated by whole body's motion in case when vision was spared or excluded. These neurons were heterogeneous in their responses to perceived movement. Some neurons were modulated by linear or axial motion, other by optokinetic stimuli and some of them by combination of these stimuli. Direct evidence about the importance of vestibular stimuli in spatial navigation came from experiments with passive rotation in both dark and light sessions. In session with passive

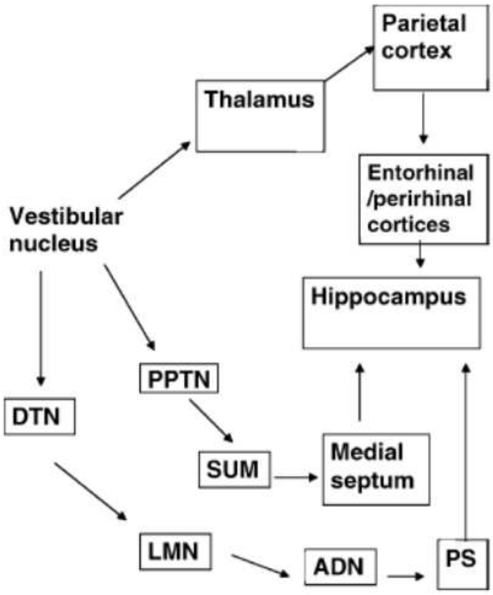


Figure 2.0.8: *Some potential pathways from the vestibular nucleus to the hippocampus. Abbreviations: DTN, dorsal tegmental nucleus; PPTN, pedunculopontine tegmental nucleus; SUM, supramammillary nucleus; LMN, lateral mammillary nucleus; ADN, anterodorsal nucleus; PS, postsubiculum.*

rotations in the dark, the optokinetic information had been eliminated. Measurements of the activity of place cells in rats showed that positions of the firing fields had been updated with respect to stable room cues after a passive rotation in darkness (Wiener et al. 1995, Sharp et al. 1995, Gavrilov et al. 1996b) as well as in light (Knierim et al. 1995). Adaptation of the firing fields in the dark was result of the robust influence of vestibular inputs (and other inertial stimuli) perceived by the animal. A solicit question is about a "hierarchy" or a "competition" between vestibular information compared to other types of stimuli (e.g. optokinetic information). Sharp et al. evaluated the influence of the visual and vestibular inputs inside the cylindrical arena with independently movable floor and wall. When both vestibular and optokinetic stimuli were present consistently (i.e., perception of the movement was accompanied by inertial stimuli from the floor rotation and from the optic flow by means of optic movement from the wall), a predictable shift of the firing fields was observed. Conversely, when the position of the floor was stable and the wall rotated, predictable shift of firing fields was disrupted and place cells became bound to the stable floor rather than to the rotating wall. These results emphasized the importance of an "anchoring" of spatial information from visual system with respect to vestibular inputs. However, with increased experience of "unexpected" rotations, the probability of predictable shift has also increased, suggesting learning component in the hippocampal neural network. Nonetheless, another appealing question is, how precisely and robustly vestibular inputs modulate spatial information.

"Inertia" and head direction cells HDS exert an important role in the processing of "compass" or "directional" type of spatial information which is independent of the location and actual behavior of the subject. Structures containing HDC are rather extensive and interconnected with other areas in the brain. They receive highly pre-processed multimodal sensory and motor information. Generally, vestibular system seems to be important for modulation of HDC signal, together with motor and proprioceptive systems. Several studies reported importance of interplay between the VS and HDS. Stackman and Taube (1998) showed that directional signal in the HDC in anterodorsal thalamic nucleus (ADN) was abolished by neurotoxic lesions of the vestibular labyrinth for at least 3 months after lesion. Subsequent studies have also found similar effects in other brain structures, e.g., postsubiculum. Experiment of Stackman et al. (1998) showed a noteworthy fact that impairment of the HDC signal persisted despite the fact that landmark cues or optic flow were present and HDC signal had become fixed to them before the lesions of VL . Disrupted activity of the HDC was likely not a result of abolished activity of secondary afferent vestibular neurons. Activity of these neurons has returned back after several hours after lesion (Ris and Godaux, 1998) and this did not ameliorate deficient directional activity in the HDC. Head direction cells, which had been disconnected from the VS, still appeared to be functionally organized. As discussed above, HDC in an intact brain are most likely organized in the ring-like attractor network. Studies of Muir et al. (2009) showed that when vestibular system is ablated, neurons in ADN still behave in accordance with attractor model, but directional specificity of the neurons became random.

Anatomical interconnections between the HDC and the VS go through lateral mammillary bodies (LMB). Inputs from LMB project to ADN and by means of postsubiculum to the entorhinal cortex (see Fig.1.2.5).

Vestibulo-visual cooperation

Generally, a challenging question is what are mutual interactions between sensory stimuli which code the information from the environment or inner body. This sensory information can arise from the same (e.g. optic flow vs. information about visual landmarks) or different sensory modalities (e.g. auditory information vs. visual information). When animals or humans are actively moving or passively transported, they perceive the above-mentioned visual or vestibular inputs derived from active/passive movement. These two sensory modalities are often present together and there must be some mechanisms of cooperation between these stimuli, which ultimately serve the same output. From an anatomical point of view, vestibular and visual signals interact at several brain levels (see tab. 2.3).

It is presupposed that vestibulo-visual interaction in the perception of motion is not "stationary" but dynamic process. Brandt et al. (2005) used PET and fMRI methods for studying the vestibulo-visual interactions. The authors discovered reciprocal inhibition between sensory areas which process information from vestibular and visual system in humans. When one type of information about self motion dominated, brain areas represented less dominating source of information about self-motion was inhibited . The authors believed that such interaction allows a potential mismatch between two incongruent or misleading sensory stimuli to be suppressed by shifting of sensory weights to the dominant or more reliable modality.

		Experiments showing vestibulo-visual interaction
Authors	Species	Anatomical structures and functional interaction
O'Mara et al. (1994)	monkeys	Three types of neurons from the complex of vestibular nuclei were sensitive only for vestibular or optokinetic information, or both of them, when the animal was moved in a rotable drum arena, or when the animal was sitting and movable wall rotated around the animal.
Brandt et.al (2002)	humans	Caloric stimulation of the vestibular system activated parietoinsular (e.g.vestibular) cortex and inhibited occipital cortex and *vice versa.* Optokinetic stimulation activated the visual system and inhibited the parietovestibular cortex.
Sharp et al.(1995)	rats	Two groups of a place cells in the hipocampus were found: First, smaller group selectively represented cues bound to optokinetic stimuli generated by rotating drum-shaped wall, while the floor of the arena was stable. Second group was fixed to stable walls while the floor was rotated. Arena rotation generated inertial forces, which could be perceived mainly by vestibular inputs.

Table 2.3: *Examples of studies demonstrating relational interactions between the visual and vestibular system on different brain levels.*

2.0.7 Moving targets

“Thus we may have knowledge of the past and cannot control it; we may control the future but have no knowledge of it”

Shannon, 1959

“Approach” and “avoidance” behaviors

Animals and human naturally interact with moving object occurring in the environment. We can find many examples of approach behavior (see Table 2.4). Predators need to adopt a suitable strategies for an effective hunt and many animals approach the members of the same social group in order to fight or approach a partner during mating. Approach behavior can be categorized into several patterns. Beside approach behavior, animals often avoid predators or members from the same social group that are situated on higher level of social hierarchy. Another example of avoidance behavior is avoidance of an obstacles during walking or running, because animals or humans might represent obstacles relatively as bound to a "body-like" frame and being “movable” with respect to their trunk axis. Avoidance of an object or a place in space fundamentally differs from approach behavior. Effective avoidance could be realized by navigating to a “futhermost” place rather then target, or to some restricted place defined by target. Conversely, approach behavior requires continuous reduction of a distance between the target and the subject. In spite of this well-described phenomenological distinction, the neural mechanism for avoidance and approach behaviors are not clarified yet and it is not even clear whether these neural mechanisms are the same or similar for both types of navigation.

Approach behavior	Avoidance behavior
hunting a pray	*avoiding a predator*
chasing toward a mate	*avoiding a collision with an obstacle (stable or moving)*
flying subject landing to a goal place	
playing ball games	

Table 2.4: *Examples of approach and avoidance behavior*s

Processing of information about a moving target is naturally limited of physical constraints of our sensory modalities, synaptic delays between neurons in successive neural stages or also by the fact that our brain perceives and processes 3D objects projected on retina as a 2D image. This phenomenon is called inverse problem of vision (Palmer et al.,1999) and historically there are two main theories which had tried to explain how brain solve this perceptual difficulty (Zago et al., 2009). The first one, co-called Ecological theory (Gibson, 1979) presumes balance between perception of the environmental and agent components of the ecosystem and relies heavily on biological adaptation mechanisms required to meet goals crucial for the agent's survival (Shaw et al. 1982; Shaw 2003). Organisms may directly interact with their environment and other objects by means of their senses and directly react to the actual situation without computations or internal memory representations (Zago et. al 2009). Visual information about objects can be represented by optic patterns (texture gradients, spatial occlusion, motion parallax, focus of expansion or rate of expansion). Interception task may be a typical example of a such perception, because all perceived information processing required for estimating position of an object takes place online and immediate response to them lead to a successful interception. However, recently this theory has been revisited to account for importance of extra-retinal information and role of central processing of visual information. Zago et al. (2009) concludes in his review that "the recent point of view is that several kinds of information either or alone can afford estimates about location and time of potential contact with an approaching target" (Zago et. al 2009, see also Hecht et al., 2002). A contradictory Constructivism theory presumes reconstruction of incomplete

Interception activities in the research
Interception of flying vertebrates and insects - interception in 3D space.
“Walking” or “running ” subjects chasing for another target - interception only in the horizontal plane.
Interception in ball-game players - interception in the vertical plane or in both planes. Effects of the gravity.
Manual hitting of a target - highspeed inerception of moving projectile.
Eye pursuit tracking - Measuring saccadic eye movement with respect to rapidly moving targets.
Robotics - interception of moving targets, e.g. robotic ball games

Table 2.5: *Interception of moving targets in different areas of research*

information by higher sensory centers and stages (Helmotz 1867, Shepard 1984). According to this theory, internal representations enable prediction of future arrangement of the spatio-temporal trajectory of the actually seen moving target. Despite the fact that experimental paradigms studied interception strategies in many animal species, humans (or even in robotics), it is possible to divide these strategies into several subgroups (see Table 2.5), Only relatively small number of variables can be defined which are important for characterizing computational processes of interception (see. Fig.2.0.9). These variables are “cornestones” and determinants for characterizing basic behavioral patterns. It is worth to notice that an animal species can use more interception strategies even in one interception episode (Collet and Land, 1978). We can assume that an important factor for interception process is sensory and computational equipment of the organism’s nervous system. Speed of the target to which interception occurred, i.e. available time period for proper interception, is another important variable. Next part of this section will shortly summarize selected basic interception strategies.

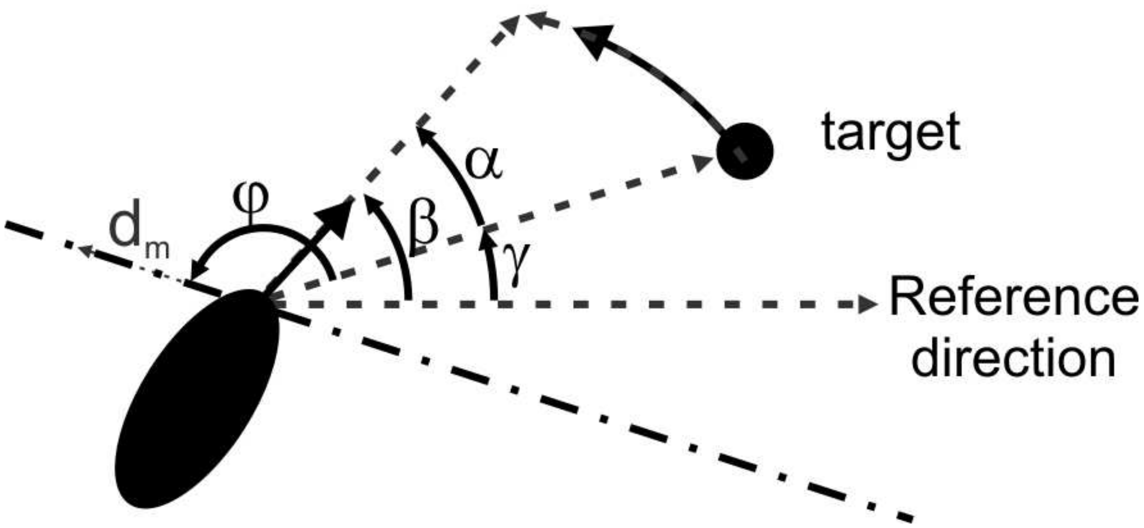


Figure 2.0.9: *Some basic parameters crucial for subjects (represented by a big black elipsoid) intercepting a moving target (small black circle). Angle* α *is defined as an angle between vector of subject´s movement and line connecting it with center of gravity of the target. Angle* β *is defined as an angle between the direction of the movement and some reference direction in the environment. Angle* γ *is defined as angle between a reference direction and the line connecting the subject´s head and the target´s center of gravity.*

Strategies of interception

Generally, most of the literature predominantly demonstrates cognitive mechanisms of approach behavior rather than avoidance behavior. Approach behavior can be categorized from several points of view. It is obvious that character of the interaction with goal to approach is dependent on a time range available for approaching. If a subject had to hit some very rapidly moving target, the whole process would last only several milliseconds. For such interactions there is too little time for correction of catcher's trajectory. It is usually assumed that during short and quick interceptive events, subjects predominantly use prediction strategy to estimate future place of contact in an accurate timescale. In this case, the subject estimates future position of contact only from initial information about the position and speed of the target - this is called open-loop strategy. If the target moves slowly or quickly, but on a longer trajectory, then the subject usually have relatively more time for updating actual information about the position and speed; i.e. it can analyze step-by-step the actual information inputs and react to them by appropriate motor output. This is the case of so-called closed-loop strategy. In one example of such case a catcher (e.g. a baseball player or hunting bat) runs or flies on a long-trajectory and correct its own position or a speed profile of its movement. Several strategies have been proposed to explain target-approaching behavior in various animal species. Selection of strategies depends on many variables of sensory equipment of the subject, especially its visual system. Generally, strategy depends on 1) mutual position between target and subject (see Fig. 2.0.10, part I.), 2) direction of movement 3) speed of the target 4) movement abilities of the subject to reach the target and 5) on actual conditions inside an environment, e.g. presence or absence of a) obstacles b) stable or moving landmarks or objects – these may burden the visual system, compete with target and even block interception trajectory, or c) geometry and shape of the environment which can influence movement inside the environment. There are two basic approaches to intercept the moving target. “Knowing how to get there” and “Knowing where to go”.

Knowing how to get there - *Pursuit strategy* “Knowing how to get there” does not presume subject’s knowledge about a future target position, but subject can select the strategy which brings him to the target step-by-step. This strategy requires certain level of sensory feedback for actual correction of output of the subject in face of dynamically changing sensory inputs.

A subject can move directly towards the target. This strategy is called pursuit or tracking strategy. It has been reported in teleost fish Acanthaluteres spilomelanurus as the preferential strategy (Lanchester and Mark, 1975), in chimpanzees (Pan troglodytes), especially at the beginning of the training (Iversen and Matsuzawa, 2003) and in humans in cases when the target moves slowly (Rushton et al. 1998). This strategy is not computationally difficult and requires 1) higher speed of the subject pursuing the target, 2) maintaining the target heading at zero (see Fig. 2.0.10, part II.).

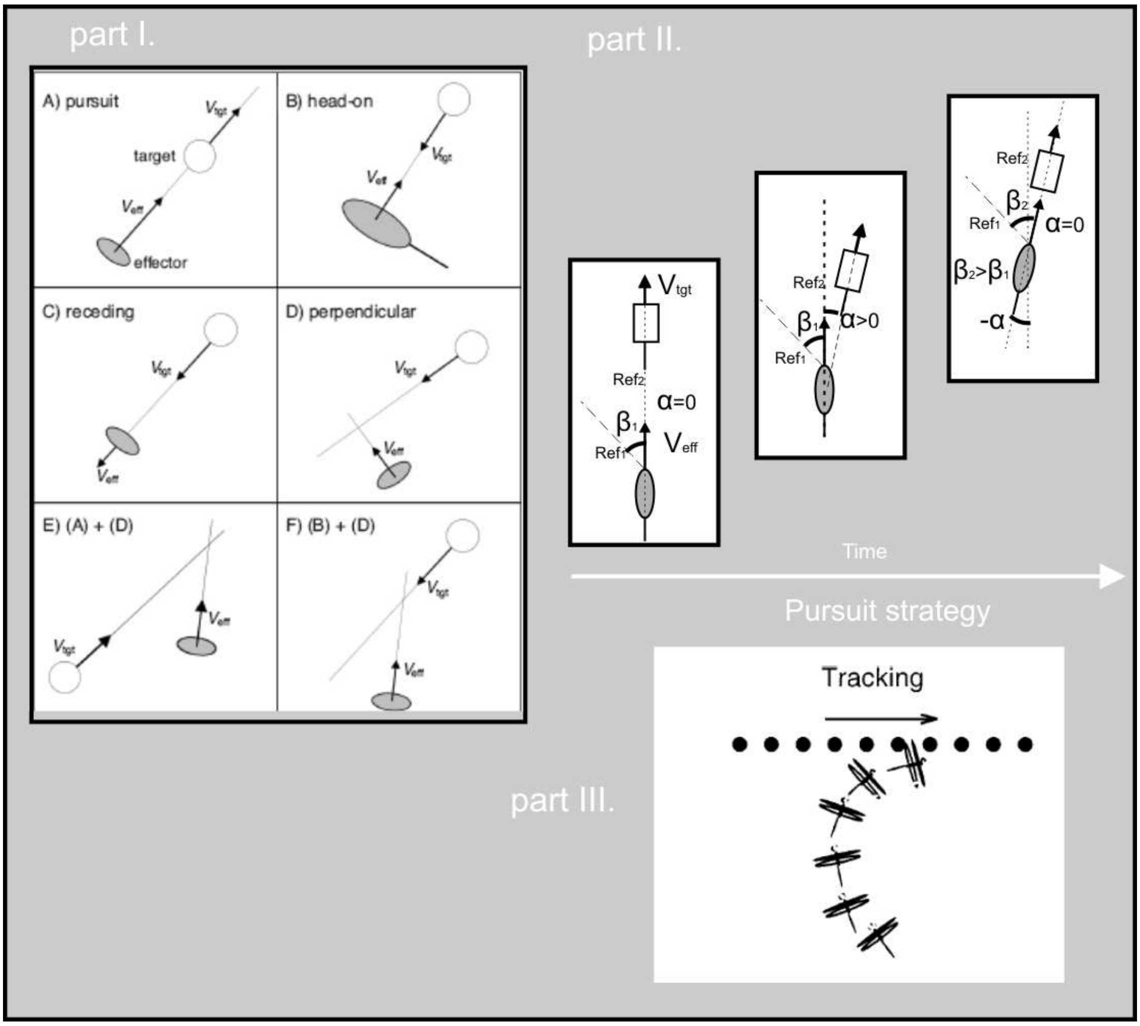


Figure 2.0.10: *Part I: Simple models of interception. A - Pure pursuit configuration. B - Head-on collision configuration. C - Receding configuration, in which the target heads towards a slowly moving effector. D - Perpendicular approach configuration. E - Vector combination of pursuit and perpendicular configurations. F - Combination of head-on and perpendicular configurations.(from Tressilian, 2005). Part II: Scheme of a pursuit strategy. Subject continuously nulls the angle*α *(between the vector of velocity and the target), while the angle* β *(angle between the vector of velocity and reference direction) is not controlled and changes randomly. Part III: Scheme of a trajectory of pursuiting insect, suggested by Collet and Land (1978).*

Knowing how to get there - *Keeping a constant angle* Most widely accepted model for interception is constant bearing angle model, and this strategy was used for a long time by sailors for avoiding collisions with landmarks (Le Brun 2002). This strategy is optimal when target moves along a direct or constant trajectory. In this strategy, the subject keeps the angle between its heading (velocity vector) and the target constant (Lenoir et al. 1999, Chardenon et al. 2004, Ghose 2006), (see also on angle α in Fig.2.0.9 and Fig.2.0.11). Alternative nomenclature also exists, when subject keeps the angleα constant - ***Constant Target-Heading Angle Strategy***, *CTHA*). Yet another type of the strategy involves the orienting angle γ constant (Fig. 2.9 angle γ and Fig. 2.0.11), called (***constant absolute target direction strategy***, *CATD*).

If the target moves along a straight line then these strategies result in a straight trajectory of the subject. The condition necessary is that α or γ are set in such a way that the distance between the subject and the target decreases. Subject naturally does not have to adjust these angles constant continuously. It is sufficient if it compensates for changes in these oriented angles. Advantage of these strategies is that they are computationally simple and errors in the estimation of α or γ are corrected during navigation. In addition, unexpected changes of target's movement are compensated as well. Experiments demonstrated that humans null changes in α andγ if they approach a target moving along a linear trajectory (Fajen and Warren, 2007; Lenoir et al. 2002). Ghose et al. (2006) studied how bats *Eptesicus fuscus* chase an erratically moving insect. The authors concluded that the bats had nulled changes of γ (CATD strategy).

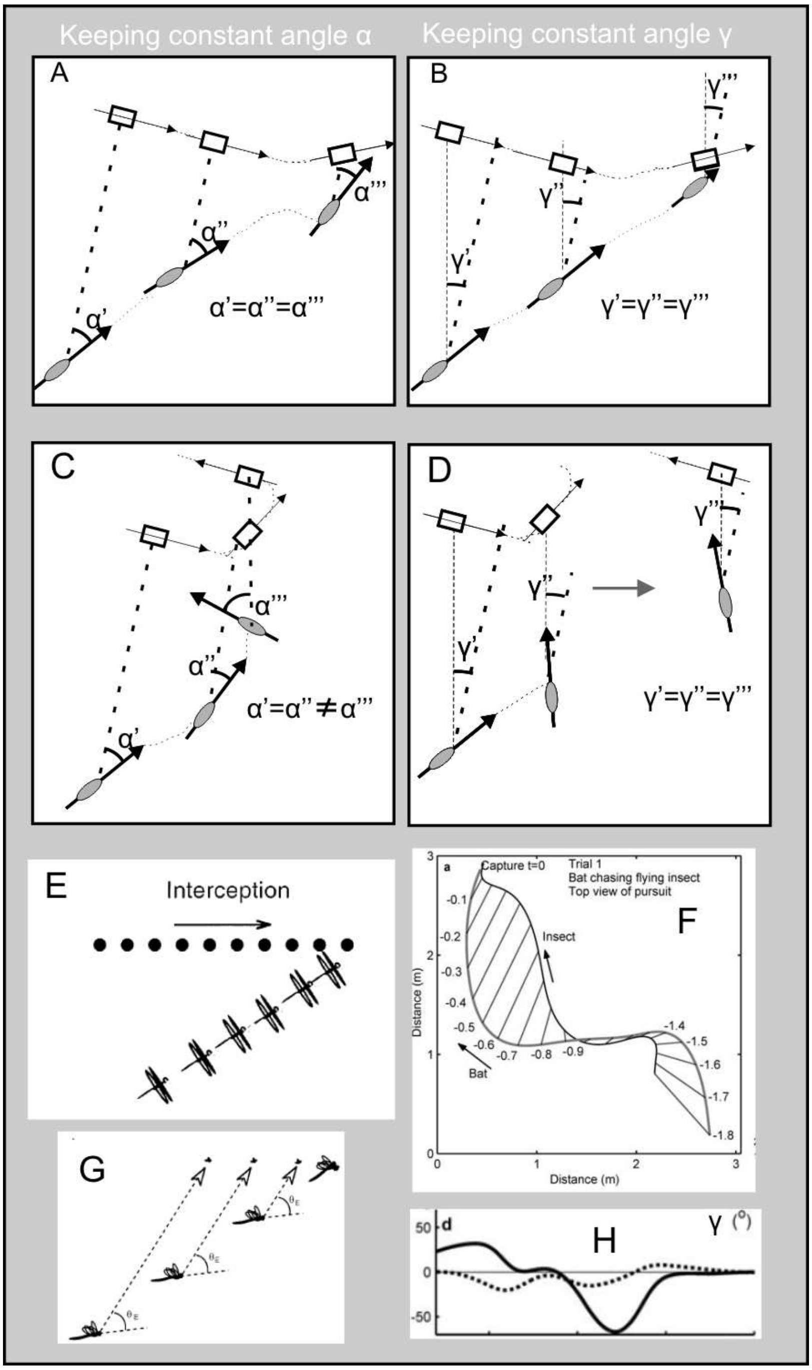


Figure 2.0.11: *A: Keeping a constant angle* α *is most effective in trajectories which are straight E) or periodical. In G), an example of this strategy in dragonfly is shown (adapted from Olberg et al. (2000). C) When the target moves erratically, this strategy is not suitable, and the trajectory of the subject is obviously "jumped" of the track and the trajectory of the subject has a loop-like form. B) In contrast, keeping a constant angle* γ *allows the subject to regulate its heading flexibly and intercept an eratically moving target. F) shows trajectories between a bat and a erratically moving pray, in H) course of the angle*γ *in both horizontal (solid line) and vertical (dotted line) plain is plotted (adapted from Moss et al. (2006).*

Knowing how to get there - *Keeping constant changes of an angle* Other strategies were also proposed to explain the ability of humans and dogs to catch a flying ball – optic acceleration cancellation strategy (OAC) (McLeod et al., 2003; McLeod et al., 2006) and linear optic trajectory strategy (LOT) (McBeath et al., 1995; Shaffer et al., 2004). The LOT strategy is not applicable in the situation in which the target as well as the pursuer moves in a single plane. The OAC strategy or generalized OAC strategy requires that the subject guides his/her movement in such a way that the angular elevation of the ball increases with decreasing rate and the horizontal angle (Fig.2.0.12) between the direction from the fielder toward the place where the ball projects on the ground and a reference direction increases with increasing, constant or decreasing rate depending on the lateral velocity of the ball movement. It is not clear whether humans can estimate the angular accelerations with enough precision nevertheless the OAC model fits the observed trajectories well (McBeath et al., 1995). It has been reported that different strategies can participate in a single pursuit trajectory (Regan, 1998).

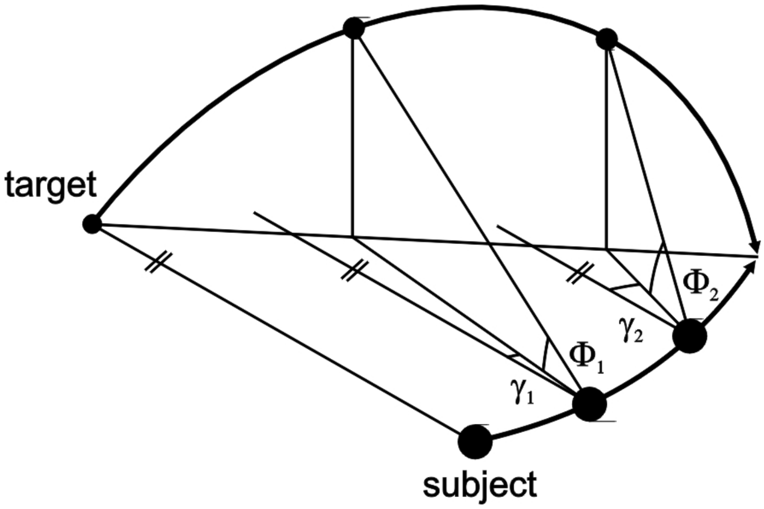


Figure 2.0.12: *Scheme of two hypothetical strategies in which the interception is coupled with regulation of change of the angle between the subject and moving target. Ball catchers are moving so that ϕ increases with decreasing speed and γ increases with a constant rate (Optical Acceleration Cancellation Strategy, OAC). An alternative strategy presupposes that $d\phi\ /d\gamma$ is constant and both ϕ and γ are increasing (Linear Optical Trajectory Strategy, LOT) from Blahna and Klement (2008).*

Knowing where to go - *Predictive strategy* This strategy presupposes that the subject knows in which position the target will arrive during a given time and this strategy is usually used for "rapid" interception events. This strategy involves higher-level computational process than above-mentioned strategies. Information can be processed in the initial phase of interception and usually does not require any sensory feedback, subjects directly navigate toward a place of meet with the target.

Animals frequently intercept a moving target along straight trajectories – howerflies *Eristalis* and *Vollucella pellucens* (Collett and Land, 1978); dragonflies *Erythemis simplicicollis* and *Leucorrhinia intacta* (Olberg et al., 2000; Olberg et al., 2007); teleost fish *Acanthaluteres spilomelanurus* (Lanchester and Mark, 1975); archer fish *Toxotes jaculatrix* (Rossel et al., 2002); chimpanzees *Pan troglodytes* (Iversen and Matsuzawa, 2003). One of the possible underlying strategies is predictive strategy. Based on the information perceived during a short period of time the subject calculates future positions of the target and moves to the predicted place of contact. Thus it keeps constant heading direction. Rossel et al. (2002) showed that archer fish use predictive strategy to catch a falling prey.

The predictive strategy has limitations, especially if it is used for long intervals (Regan 2003). It requires that the variables upon which the prediction is made are precisely estimated and that the target does not change its movement. For these limitations predictive strategy or preprogrammed movement is used to explain target-approaching behavior in situations when there is no time for perceptuomotor feedback (Tresilian, 2005).

Brain and the moving targets Generally, there exist only a few studies in various animal species, showing roles of different brain structures engaged in processing of moving targets. These structures were described in sensory, associative and motor systems at different levels of information processing. For example, target selective descending neurons from dorsal parts of dragonfly eyes seem to be involved in interception (Frey and Olberg, 1995). These neurons are interconnected with neurons for coordination of flying. In archer fish (*Toxotes jaculatrix*) a small group of Mauthner cells from reticular formation is responsible for fast and accurate predictive behavior (Fetcho et al. 2004, Schlegel and Schuster 2008). In a toad (*Bufo bufo*), hunting flying insect, an engagement of hypothalamo-striato-cerebellar circuit in motor and regulatory components was shown (Finkenstäd and Evert, 1988).

Recently, several electrophysiological studies on monkeys have brought a consistent view how nervous system processes information about a moving target. Neurons whose activity was sensitive for monitoring moving targets were reported in supplementary eye fields. Subgroups of these neurons were sensitive to expectations of change of target movement (Heinen 1995). These subgroups represent different expected direction of target's movement. They compete against each other (Hemptinne et al. 2008). Eskandar and Assad (2002) also found neurons in lateral intraparietal cortex (LIP) with firing specificity for direction of a moving target. Interestingly, these neurons were active hundreds of millisecond before the movement started. The authors interpreted these findings as prediction of the upcoming direction of the target motion (Eskandar and Assad 2002).

Despite spatial behavior has been extensively studied in rodents, there is a lack of studies exploring interaction of rodents with moving targets (Klement et al. 2008, attached in the thesis). It is still an open question whether rodent positional and head direction systems play an important role in processing of information about moving targets. Functions of these systems have been studied in detail in a stable environment. Only a few studies addressed the role of these systems in moving environment (Klement et al. 2008) but only one recorded hippocampal neurons while rats interacted with a moving object (Ho et al. 2008). Ho and his colleagues trained the rats to be close to the moving object. It is a very simple behavioral model of mutual interaction between a rat and a target. Despite the neuronal activity was analyzed in detail, the behavioral aspects were studied rather superficially.

Part II

Aims of the dissertation

Despite intense research into spatial behavior, most of experiments done in animal species and humans exploited stable world conditions. However, world is rather dynamic than stable and is composed by time changes between positions of targets or places. In general, we can ask if living organisms perceive and process stable and dynamic world in the same manner and which brain structures are necessary for processing of the dynamic world. We can also search for differences of navigation strategies for dynamic or stable world. The literature summarized above shows that despite many experiments in dynamic environments performed in various animal species and humans, only few of them use laboratory rats as a model organism. Nevertheless, rats and rodents generally are useful biomodels for studying relationships between specific types of behavior and brain structures, which provide neural substrate for these behaviors. We therefore decided to evaluate behavior in a dynamic environment in three different paradigms. First paradigm tested behavior of rats in a modified carousel maze (also known as the AAPA task, see Figures 2.0.4 and 2.0.5), where solely the inertial inputs available to animals were manipulated while keeping other factors constant. In next two paradigms we evaluated spatial behavior of rats in the environment with moving target involving "escape" or "approach" model of behavior. Yet another study aimed at testing the hypothesis that parietal cortex lesion would produce selective deficit in the spatial avoidance defined either by distal visual cues or by proximal marks on the arena. Main aims of the dissertation were the following:

1. **Evaluation of the role of inertial stimuli for spatial behavior in the dynamic world on the carousel arena**
2. **Development of a suitable spatial task involving dynamic world, in which rats interact with a moving object.**
3. **Testing the hypothesis that posterior parietal cortex is necessary for spatial avoidance of an unmarked place defined by proximal or distal cues.**
4. **Testing the hypothesis that rat hippocampus is necessary for processing of information about an aversively reinforced moving object (i.e. mobile robot).**

5. Assessment of behavioral strategy, which is used by rats during navigation towards a moving target in a modified water maze task.

Part III

Methods

Animal welfare and manipulations

Subjects

The subjects used for experiments were male adult Long-Evans rats obtained from the breeding colony of the Institute of Physiology, AS CR. All animals were three-month-old at the beginning of the each experiment and weighted between 250 g and 300 g. They were housed in groups of two to three per cage in a temperature-controlled animal room (20 - 22°C) with a 12/12 hours light/dark cycle with light on at 7:00. Food and water were freely available. The rats were accommodated in the animal room at least for 10 days before the experiment started. All experimental procedures were carried out during the light period of the cycle. The procedures were in accordance with guidelines of the Animal Protection Act of the Czech Republic, National Institutes of Health (NIH) and with the directive of the European Communities Council (86/609/EEC).

Initial manipulations with the animals in aversively motivated experiments

In general, we have used aversively motivated behavioral procedures. Rats which were trained to avoid denied sector on the carousel arena or denied circular sector defined by the position of moving object undergo some common procedures. Each animal was handled by the experimenter for two to three minutes onn three consecutive days. After the last handling day, rats' skin on the neck was pierced by a hypodermic needle. The sharp end of the needle was bent into a closed loop in order to prevent the needle from slipping out of the skin. The procedure was carried in awake rats as they tolerated this procedure well. During training sessions the needle was electrically connected to the device for delivering electrical current by a wire.

Carousel arena

In the main part of this section was evaluated the importance for learning process of the inertial stimuli, generated by the rotation on the carousal arena task.Original data were alredy published by the authors Blahna et al. (2011). The original manuscript is attached on this thesis.

Second study on the carousel arena task has evaluated the role of the posterior parietal cortex in the carousal arena task. Method and most important results from the study were adapted and modified from the original paper written by the authors Svoboda et al. (2009). Manuscript is attached on this thesis.

2.1 Inertial stimuli in the carousel arena task

2.1.1 Apparatus

The apparatus consisted of a circular arena (diameter = 79 cm) surrounded by an annular belt (inner diameter = 80 cm, outer diameter = 130 cm) (Fig.2.1.1). The arena and the belt could be rotated independently of each other by two electromotors located below the arena and below the belt. The arena wall (height = 40 cm) was transparent. The belt wall (height = 100 cm) was a black curtain completed above with a black annular board (inner diameter = 65 cm, outer diameter 130 cm) (Figure 2.1.1). The belt, the black curtain and the black annular board formed an enclosed space around the arena. A subject on the arena could see only a part of the ceiling of the experimental room right above the arena through the opening in the annular board. Three salient cues were attached to the black curtain. A white card (width = 42 cm, height = 55 cm) was on the west 34 cm above the arena. Another white card of the same size was on the northeast 38 cm above the arena. A lamp was located on the east 80 cm above the arena. The lamp was the only source of light in the experimental room. It illuminated the enclosed space around the arena. There was a camera located above the arena. The camera was connected to a computer-based tracking system (iTrack, Bio-Signal Group, USA) located in an adjacent room. Since the arena or the belt rotated during experiments, a subject's position on the arena could be represented with respect to the reference frame defined by the arena or with respect to the reference frame defined by the belt. The computer-based tracking system recorded both positions with 40 ms sampling rate by tracking two infrared light emitting diodes. One diode was attached to a subject on the arena, the other was attached either to the arena or to the belt depending which part of the apparatus was rotating. Tracking the second diode made it possible to calculate position of a subject with respect to the rotating reference frame. The computer-based tracking system also controlled a device for delivering electrical current. When activated, a subject felt an aversive stimulus on its paws.

2.1.2 Behavioral training

The rats (n=14) were habituated to the arena in 5 to 8 min sessions carried out in two consecutive days. The arena and the belt were stable during the habituation sessions. The animals could freely explore the arena as no aversive stimuli were delivered. After the habituation sessions the rats were randomly divided into two groups of equal size (Groups A and B). The groups were trained either in the 6 standard active place avoidance task or in a modified active place avoidance task. Group A was first trained in the standard task for six days (Phase 1) and then in the modified task for four days (Phase 2). The training in the modified task lasted only four days because the rats mastered it already in two days. One rat from Group A (rat -12) learned slower, therefore, it was trained in both tasks for six days. Group B was first trained in the modified task for six days (Phase 1) and then in the standard task for another six days (Phase 2). One rat from Group B (rat -8) was trained in the standard task for only four days. This rat solved the modified task as good as the standard task already in the first session of Phase 2. The to-be-avoided sector was located on the South of the belt (azimuth 180) in Phase 1 and on the North-Northeast (azimuth 22.5) in Phase 2. The rats were trained in one 20-min session each day.

2.1.3 Standard active place avoidance task

In the standard active place avoidance task the rats were trained on the rotating arena to avoid a 60° wide hidden sector defined in the reference frame of the belt (Fig. 2.1.1B). The belt was stable. The arena rotated clockwise one revolution per minute. The rats could move freely over the arena, however, they received aversive stimulus (electrical shock) after entering into the to-be-avoided sector. The entrance into the to-be-avoided sector was counted if a rat stayed there for at least 0.5 s. The electrical shock had intensity 0.4 mA and lasted 0.5 s. If the rat did not leave the sector then the aversive stimulus was repeated every 1.5 s. A new entrance into the to-be-avoided sector was counted after the subject has been outside of the sector for at least 1.5 s.

2.1.4 Modified active place avoidance task

The modified active place avoidance task was identical to the standard task except the arena was stable and the belt rotated around it (Figure 2.1.1 C). The belt rotated counter-clockwise with speed of one revolution per minute.

2.1.5 Data analysis

Rats' trajectories in the arena frame and in the belt frame as well as times of delivery of aversive stimuli were analyzed using MatLab functions written by the authors. We evaluated four commonly measured variables which have been previously shown to characterize behavior in the active place avoidance task well. They were *number of entrances* into the to-be-avoided sector, *maximum time spent outside the to-be-avoided secto*r, *time to the first entrance into the to-be-avoided sector* and *path length.* We used t-test, one way ANOVA with repeated measures and two-way ANOVA with repeated and non-repeated measures for statistical analyzes. If needed, Tukey's post hoc test was used for multiple comparisons. The level of significance was set to 0.05. To make the distribution of the variables more similar to normal distribution and of similar variances, the variables were

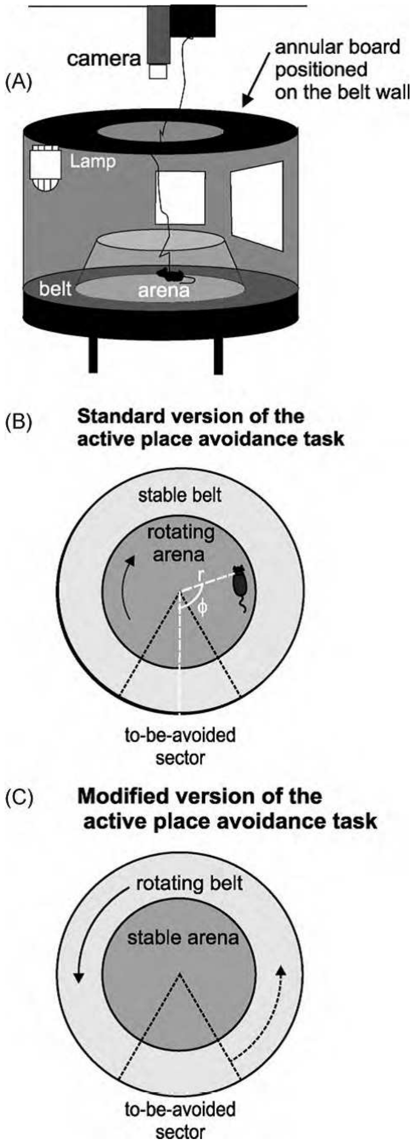


Figure 2.1.1: *A. Behavioral apparatus. B. Schematic illustration of the standard active place avoidance task (Carousel arena). A rat on the rotating arena was trained to avoid a 60-deg sector defined with respect to stable belt. C. Schematic illustration of the modified active place avoidance task. A rat on the stable arena was required to avoid a 60-deg sector defined with respect to the rotating belt (Adapted from Blahna et.al, 2011).*

trans formed before statistical testing. Number of entrances (N) was transformed to log (N+1), maximum time avoidance (Tmax) was transformed to log (Tmax) and time to the first entrance (T1) was transformed to log (T1 +1). No trans formation was used for path length (L).

2.2 Role of the posterior parietal cortex

2.2.1 Surgical procedures

Rats were operated like a sham-control group (control, n = 10) or like a posterior parietal cortex lesion (parietal, n = 10) group. Rats were anesthetized with xylazine (40 mg/kg, i.p.) and ketamine (50 mg/kg, i.p.) and than placed in Kopf stereotaxic frame. The skull was exposed and two openings were drilled into the skull to expose the brain at the following coordinates relative to the bregma: AP −0.5 to −5.5, L 1 to 6. Bilateral thermocoagulation lesions of PPC were made by applying the tip (diameter = 0.5 mm) of a calibrated soldering iron (temperature 180 °C) directly to the dura mater for 0.5 s at various points within exposed area until the entire surface was touched. Sham-operated rats underwent the same procedure except for applying the soldering tip to the dura. The thermocoagulation lesions were previously shown to be effective and safe for the animals (Save and Moghaddam 1996, Save et al. 2000). Sterile gelfoam was then placed in the openings and the wound was sutured, followed by local application of lidocain and an antiseptic. The rats were then left 14 days to recover.

2.2.2 Behavioral procedures

Two variants of the carousel arena were used. In first variant the to-be-avoided sector was defined by the reference frame of the arena. Arena sector rotated together with the arena (See Fig. 2.0.5 A). Animals were trained to avoid the sector in darkness. Animals were motivated to explore the arena by search the pellets scattered from the feeder located above the arena. In second variant animals were trained to avoid the to-be-avoided sector defined by the room reference frame. Principle of this version was already described in (See Figures: 2.0.5 B, 2.1.1 B).

2.3 Enemy Avoidance Task

2.3.1 Apparatus

An experimental arena is described in Fig 2.3.1. Experiments took place on a circular featureless arena (diameter 85 cm) elevated 1 m above the floor. The arena was enclosed by a 50-cm-high dark black paper cylinder to eliminate any disturbing effects of the extramaze environment. An electrically grounded floor was made from fine wire mesh. Both animals were released into the arena simultaneously, but to opposite positions. An overhead infrared camera mounted on the ceiling monitored two light-emitting diodes (LEDs): a smaller one, attached by a plastic strap to the back of the to-be-avoided rat (enemy rat), and a larger LED, attached to the subject rat. Coordinates of both LEDs were sampled at 50 Hz, collected by custom-made computer-based software and stored in the computer for off-line analysis. In order to motivate the rats to explore the whole environment, small pasta pellets (with average weight of 15 mg) were scattered from an overhead automated feeder over the arena every 10 s. The subject rat received a computer-controlled shock (alternating current; 50 Hz; 500 ms) through a needle connected to a shock-delivering cable whenever the distance between the two rats dropped below 25 cm for at least 100 ms. If the distance had not increased within 500 ms following the 39 footshock, additional footshocks were delivered every 500 ms, until the subject rats "escaped" from the enemy rat. Since the rats displayed considerable variability in the sensitivity threshold to electric footshock, its intensity was set individually for each rat as the lowest value to elicit negative reinforcement, but to prevent freezing. The current value used for footshocks ranged from 0.2 mA to 1.2 mA. Shocks were delivered through the implanted low-impedance needle and grounded arena floor; the highest voltage drop was between rats' paws and the floor; therefore the animals most likely perceived the shock in their limbs.

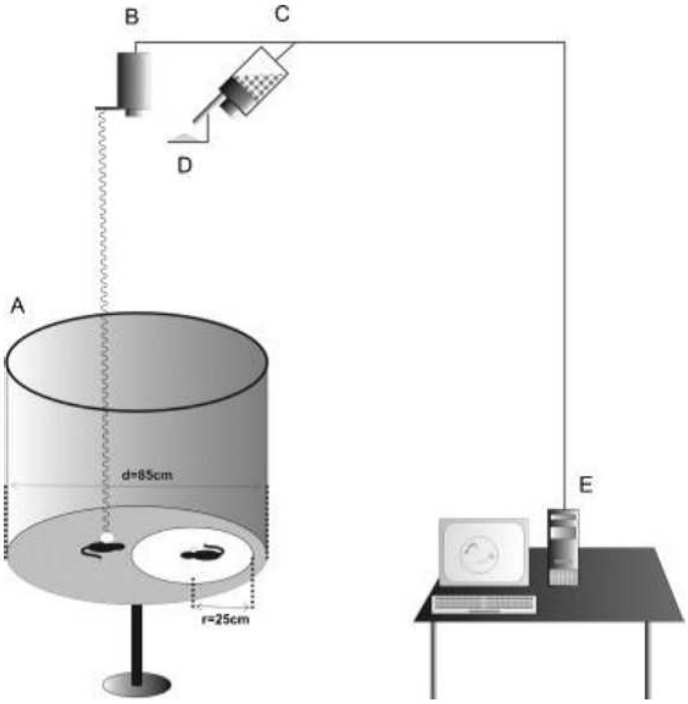


Figure 2.3.1: *The experimental apparatus used in the enemy avoidance task. (A) The experimental arena with an electrically grounded floor made of fine wire mesh. Both rats are equipped with infrared LEDs of different sizes and the subject rat (left) is connected to a computerized tracking system (E), which makes it possible to deliver mild electric footshocks exclusively to the subject animal. The Enemy rat (right) is depicted with a surrounding annulus representing the punished distance of 25 cm. (B) Infrared sensitive camera. (C) Automated feeder delivering small pasta pellets. (D) Pellet dispenser—a plastic cap with several holes ensures random dispersal of food pellets delivered by the feeder (C). Adapted from Telensky et al., submitted)*

2.3.2 Avoidance of a conspecific

Behavioral training

Rats (n = 10) were handled for 5 min daily and habituated to the arena for 5 days prior to their random assignment to subject-enemy pairs. Then, a pretraining phase of 14 days started, during which the pairs were trained to search for pasta pellets randomly scattered over the arena surface. No shocks were delivered during this phase. Each daily session lasted 20 min and was carried out between 13:00 and 18:00. Upon finishing this 14-day period, both subject and enemy groups of animals were fully habituated to the arena, i.e. they did not display any apparent behavioral marks of anxiety typical of open field spaces (such as increased level of thigmotaxis, reduced locomotion, freezing, etc.) and they learned to collect the food pellets efficiently. In the following acquisition phase (16 days) the subjects were trained to avoid of the enemy rat, which was reinforced by mild electric footshocks, delivered whenever the subject rat came or stayed closer than 25 cm. Since there was little improvement in performance within the first four sessions (regular sessions 1–4), we trained the animals the following 4 days (auxiliary sessions 1–4) with the enemy restrained to a wire mesh box, thus minimizing the possibility that the enemy actively approaches the subject. After finishing these four auxiliary sessions, we continued with the training sessions (regular sessions 5–16) under standard conditions (with enemy rat moving freely again).

Data analysis and statistics

Tracks of the enemy and subject animals were analyzed offline using a custom-based software programmed in QuickBasic 7 (Microsoft, CR) by Petr Telensky and Jan Svoboda. The following parameters were extracted from the tracks and analyzed quantitatively for subject rats: *Number of errors – number of entrances* into the punishable region (i.e., 25 cm or less from the enemy rat); *Total distance – total path length* (in meters) walked by a subject rat in every 20-min session; *Periphery dwelling – Percentage of total time spent in the peripheral part of the arena.* The periphery was defined as the outer annulus covering half of the arena surface (width of the annulus being approximately 30 cm). For analysis, animals were divided into Subject and Enemy groups on the basis of whether they received shocks or not. The number of errors per 1 m of distance and a fraction of distance traveled by subject and enemy rats in 3-s interval preceding an error was also analyzed. For statistical analysis, a one-way ANOVA was used with repeated measures on daily sessions. ANOVA was followed by a Newman–Keuls post hoc test (Statistica, StatSoft, CR) when appropriate. For comparison of Enemy and Subject groups within a session, or for comparison of either group in two successive sessions, a t-test or paired t-test was used, respectively. The significance was accepted at a probability level of 5%.

2.3.3 Avoidance of a robot

In these experiments, we modified the task: we changed the enemy rat with a neutral object with more predictable character of movement. This improved paradigm resulted in better performance of the animals to avoid the moving object. We have also examined the role of the hippocampus. The data obtained from the experiments with hippocampal inactivation are now in per-review process. The article manuscript was written by the authors Telensky et al. (2009). The manuscript was submitted and is attached to this thesis. Text of method and results were adapted and adjusted from this original paper.

The robot

The robot used in this experiment was a custom-made electronic device controlled by a programmable integrated circuit. The robot was assembled by Pavel Jiroutek, our technical collaborator and a student of cybernetics. Basic construction consists of aluminum chassis with two traction wheels on the sides of the robot, each driven by an independent electric actuator. The construction was weight-balanced and equipped with a small unpowered front wheel to ensure stability. Both traction wheels ran at equal speeds, only during turns their directions were opposite. The robot was equipped with three sensors. Two opto-isolators were attached to the wheels controlling speed and distance and a microswitch was added to a retractive front bumper. Once the bumper hit the wall of the arena, the switch was activated. Such a hit could be followed by a user-defined period of inactivity (we used 15 s to ease the task moderately). The robot then moved backwards, turned random angle and ran forward until hitting the wall again. The range of chosen angles could be limited by operating personnel (we used angles between 90 and 270°). The controls consisted of speed selectors between seven speed levels 4-28 cm/s, program switches and a remote-controlled/self-directing mode switch. Inner parts and controls were protected by removable fitting cover made of aluminum plate. A large diode was placed on the top of the robot for tracking purposes. Power was provided by five rechargeable AA type batteries. The robot was 17 cm long, 16 cm wide, and 12 cm high.

Surgical procedures

Fourteen days before the start of training procedure, were the rats under the ketamine (50 mg/kg, i.p.) and xylazine (15 mg/kg, i.p.) anesthesia mounted in a Kopf stereotaxic apparatus. Two holes in the rat cranium (1 mm in diameter) were drilled at AP -4.5, L ± 3.0 relative to bregma. Two needles (0.7 mm diam.) were stereotaxically inserted through the two openings in the cranial bone 2.5 mm below the skull surface. Both needles were fixed to the skull with dental cement. The animals were left to recover 14 days after the surgery.

Hippocampal inactivation

We used bilateral infusion of tetrodotoxin (TTX) a potent blocker of voltage-gated sodium channels for the temporal inactivation of the dorsal part of the hippocampus. One day before this procedure animals were habituated to the inactivation procedure. Forty minutes before the inactivation session on day 7 of the avoidance training, 5 ng of TTX in 1 µl of physiological saline was manually infused into each hippocampus during 1 min via an infusion cannula (0.45 mm O.D.) attached to a 5 µl Hamilton syringe by polyethylene tubing. The tip of the infusion needle protruded from the guide cannula by 1 mm, so that total distance of the infusion site from the skull surface was 3.5 mm. The infusion cannula was left in place for another minute after the infusion before it was slowly withdrawn. The same procedure was used to infuse 1 µl of saline forty minutes before the control session on day 8.

Behavioral training

All animals (n = 20) were in first part of the training habituated to the arena set-up. First two days were animals habituated 20 minutes on the arena. Rats learn to forage for barley pellets dispersed on the arena in 10 second intervals. Following habituation the animals were trained in the enemy avoidance task. In this task, the first group of rats (M group, n = 10), similarly like in a conspecific avoidance task,were trained to forage while avoiding a moving object (in this case a mobile robot). A mild electric foot-shock was used as negative reinforcement. The robot was preprogrammed to move straight forward at a speed of 10 m/s until it hit the wall. Then it waited for 15 seconds, turned within a random angle between 90 and 270° and ran again. In second group of animals (S group, n= 10), the robot was switched off and placed at the border of the arena, with its front part facing the wall. After the first 10 minutes, the robot was transferred by the experimenter to the opposite sector of the arena.

2.3.4 Data analysis and statistics

The performance of the subjects was evaluated as total session number of shocks given after entrances into the punishment circular area. Since the presence of anxious stimuli may interfere with overall degree of locomotion and spatial distribution (animals in presence of potentially stressful stimuli tend to keep to the walls of the arena, i.e. they are thigmotaxic) we measured also the total path and the level of thigmotaxis. For the latter parameter analysis, the arena was divided into an inner circle and outer annulus, having equal surface. A sampled spot was considered as thigmotaxic if it was found to occur on the 44 outer annulus. In the M and S groups, proper training took a total of 8 daily sessions. The TTX was applied bilaterally to the hippocampi on the seventh session, while saline was administered on the eighth. For statistical evaluation, a one-way ANOVA with SESSIONS as repeated measures (within subject factor) was used, followed by a Newman-Keuls post-hoc test to detect differences between particular sessions. In the PL and PS groups, proper training lasted 7 daily sessions. A two-way ANOVA with SESSION as within subject factor and GROUP as between subjects factor was used in this case, followed by a Newman-Keuls post-hoc test. All p's were accepted as significant at level $p<0.05$.

Histology

After finish of the behavioral procedures, the animals were anesthetized by ketamine. When rat were in deep level of anesthesia, we injected black ink thru the implanted cannulae which were used for temporal inactivation of the dorsal part of the hippocampus for orientational control of the distribution of the TTX. Distribution of the ink verified the localization of the infusion sites. The animals were then transcardially perfused with saline and subsequently with 4% formaldehyde solution. Brains were removed, saturated in 30% sucrose overnight, frozen, and sectioned in 50-µm coronal sections. Every tenth section was stained with cresyl violet and the locations of the infusion sites were verified (Fig. 2.7.5).

2.4 Rat interception behavior

New behavioral task testing navigation of the rats toward the moving target will be introduced . The basic strategies of navigation were tested in the pilot study. Development of the behavior and the role of the shape of the moving object trajectory were tested in the consecutive study. We also tested role of the shape of the moving target trajectory on interception behavior. This study was written by the authors Daniel Klement and Karel Blahna. The manuscript was already submitted.

Subjects

The subjects were adult male Long Evans rats obtained from the breeding colony of the Institute of Physiology, Academy of Sciences of the Czech Republic. Animals were trained in both the pilot (n=7) and the consecutive (n=5) study. They were housed in a temperature-controlled environment at 21 C°. Food and water were freely available. All manipulations were performed during the light phase of a 12/12 hours light/dark cycle. The procedures were in accordance with guidelines of the Animal Protection Act of the Czech Republic, National Institutes of Health (NIH) and with the directive of the European Communities Council (86/609/EEC).

2.4.1 Pilot study

Apparatus

The apparatus was a circular water pool (192 cm in diameter) situated in an experimental room with many cues along the walls. A video camera connected to a DVD-recorder was above the center of the pool.

Behavioral training

The rats were trained to escape from the water by reaching a moving target. The target was a piece of a white polystyrene (15 cm) held by an experimenter at the level of water surface. The target moved along the wall of the pool as the experimenter walked around the pool with the target in its hand. The speed of the target was not constant but it fluctuated either around a constant or a slowly changing value. If a rat touched the target then the experimenter took the rat out of the pool and placed it in its homecage. The interval between two consecutive sessions ranged from 15 to 20 minutes. Each rat was trained for 6 to 8 sessions per a training day. During the first 6 training days a vertical stick (1 cm in diameter, extending 40 cm above water surface) was placed in the center of the pool. The experimenter put a rat into the pool and waited until the rat touched the stick. Then the experimenter placed his hand with the target to the water surface and begun to walk. Three starting locations of the target (Northeast, Northwest, South) changed between sessions in a pseudorandom manner. The purpose of the stick was to control starting position of the rats. The rats were always at the stick when the target appeared. In the first two training days the target was stationary. The rats learned to swim to the stick making the target available and then to the target to get out of water. In the 3rd training day the target moved slower than the maximum swimming speed of the rats. We did not control speed of the target precisely as it depended on the ability of the experimenter to control his walking speed during a session as well as between sessions. Despite of it it was an easy task for the experimenter to find out whether he moves faster or slower than the rats can swim. Direction of target's movement (clockwise, counter-clockwise) changed between session in a pseudorandom manner. The rats had to swim to the stick in the center of the pool. After touching the stick the target appeared and the rats could swim toward the moving target to escape from the water. Since the 4th training day the target moved either slower or faster than the maximum swimming speed of the rats. The first daily session started with slow movement of the target. In the remaining sessions the slow and fast movement changed in a pseudorandom manner. The rats frequently did not catch the target when it moved fast. In this case the experimenter removed the target from the pool and waited until the rat touched the stick. Then the next trial began. We removed the stick from the pool after 6 training days because the rats quite frequently stopped swimming toward the target and returned to the stick in the fast sessions. We continued training without the stick for another 6 days. The rats were put into the pool and left there for several seconds. The experimenter waited until the rat swam into the opposite half of the pool to the intended starting position of the target. Then he approached the pool and started to walked along it until the rat touched the target in his hand. If the rat did not reach the target within 5 minutes the experimenter stopped his movement and waited for the rat. To eliminate trivial solution of the task in which the rat waits for the target at the wall or swims along the wall toward the target, the experimenter lifted the polystyrene and returned it back to the water surface after he passed the animal being at the wall. As before the starting positions of the target (Northeast, Northwest, South), direction of movement (clockwise, counter-clockwise) and speed (except the first daily session when it was slow) changed between sessions in a pseudorandom manner.

Data analysis

The sessions were recorded on a DVD recorder with a sampling rate of 25 frames per second. MatLab functions written by the authors were used to extract trajectories of both a rat and the target and to process them. We tracked two points on the rat (center of gravity and tip of rat's nose) and one point on the target (center of gravity). The trajectories were smoothed with a 5-point running mean. Velocity vector was calculated from the smooth trajectories as difference between two positions recorded 400 ms apart divided by the duration of this interval. From the velocity vector we calculated speed and heading direction of the rat and of the target. Rat's speed was calculated from the trajectory of the center of gravity. This ensured that the speed was small when the rat rotated on a place. All the other parameters were calculated from the trajectory of the rat's nose. The reason for this was that the nose trajectory was easier to interpret than the trajectory of the center of gravity. The rats made contact with the target with front parts. In addition they were able to quickly change movement of their front parts while their bodies tended to continue in the previous direction. As the result the intended changes in heading direction were first visible in the nose trajectory and with a delay and less clearly in the body trajectory. We calculated oriented angles α,β and γ (Fig. 2.4.1 and 2.0.9). α is an oriented angle between rat's heading direction and the rat-to-target direction.Value of α is positive if the rat swims ahead of the target movement (up to 180°). Angle β is an oriented angle between rat's heading direction and a reference direction. The reference direction was chosen as the direction from the centre of the pool to the future place of contact. For the counter-clockwise movement of the target, is positive if the rat swims toward a point on the wall which is to the left (up to 180) of the future place of contact. For the clockwise movement of the target it is the other way round. Momentary changes of dα, dβ and dγ of the corresponding oriented angles were calculated as the angular differences of two oriented angles 400 ms apart divided by the duration of this interval. We also calculated so called prediction error (Err) as the distance between the animal and the target which would arise at the moment the subject would reach the wall given its current speed and heading direction (Fig. 2.4.1). If the animal reaches the wall before the target arrives at that point the prediction error is positive. If the animal reaches the wall after the target passed through this place the prediction error is negative. The level of significance was set to 0.05 in statistical tests.

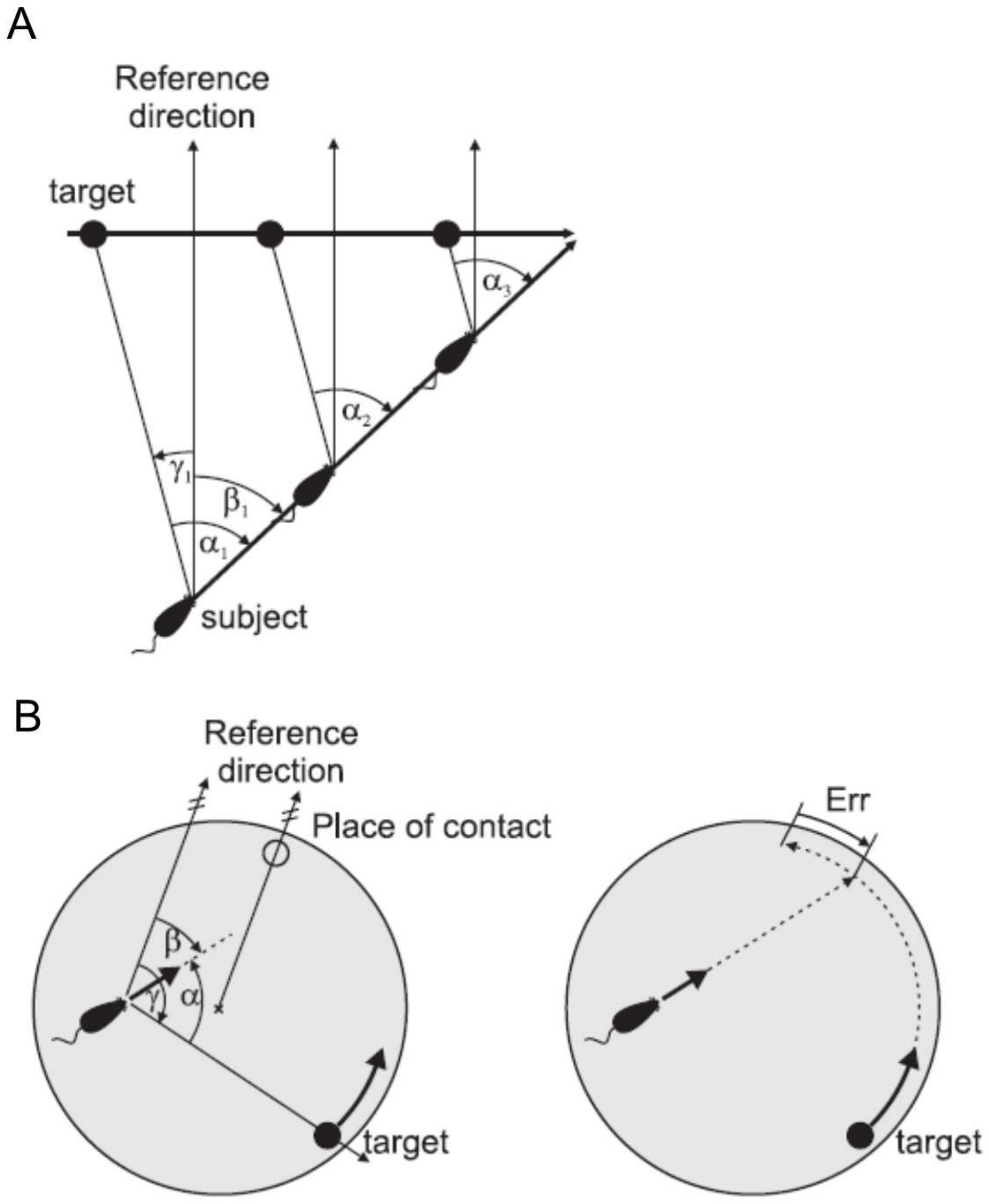


Figure 2.4.1: *Schematic illustration of navigation towards a target moving in linear way (part A) and towards a target moving along the wall of a circular maze (Part B shows the present present task). Oriented angles* α, β, *and* γ *and the prediction error Err are shown.*

2.4.2 Consecutive study

This study extended the pilot study in several aspects. First: The movable programmable platform was used. Second: We evaluated development of learning of interception. Third: We control mutual starting locations between the animal and robot. Fourth: Animals were exposed to both linear and curved trajectories of the target.

Apparatus

The apparatus was a circular water pool (192 cm in diameter) situated in an experimental room with many cues along the walls. The starting position for rat was a metal rod. The target was a remote controlled, movable robot (40 x16x 9,cm) wearing a mobile visible squared platform (12,5x 12,5x 5,cm) (figure 2.4.2). The movable robot with the platform was controlled by a remote control system. In case of an experimental sessions with a curved trajectories (CT) the robot ridden on the edge of the circular pool, in case of an experimental sessions with a linear trajectories (LT) the robot ridden on the edge of a plain desk situated inside the water pool. Color of both the wall of pool and desk was white, color the platform was black. An experiment was recorded a camera centered above the center of the pool and was connected to a DVD-recorder.

Behavioral training

The rats were trained to escape from the water by touching a platform attached by the robot. Starting positions were determinately fixed on positions schematically described in the Figure 2.4.2. A-B. If a rat touched the platform then the robot stopped its movement and the animal was taken from the water out of the pool and placed it in its homecage. The interval between two consecutive sessions ranged from 5 to 10 minutes. Each rat was trained for 20 - 24 short navigation sessions per a training day. A starting place was a vertical stick placed inside the pool. The target platform was not available at the beginning of the session. When a rat touched the stick, the target started moved and platform became available for animal by down-vertical

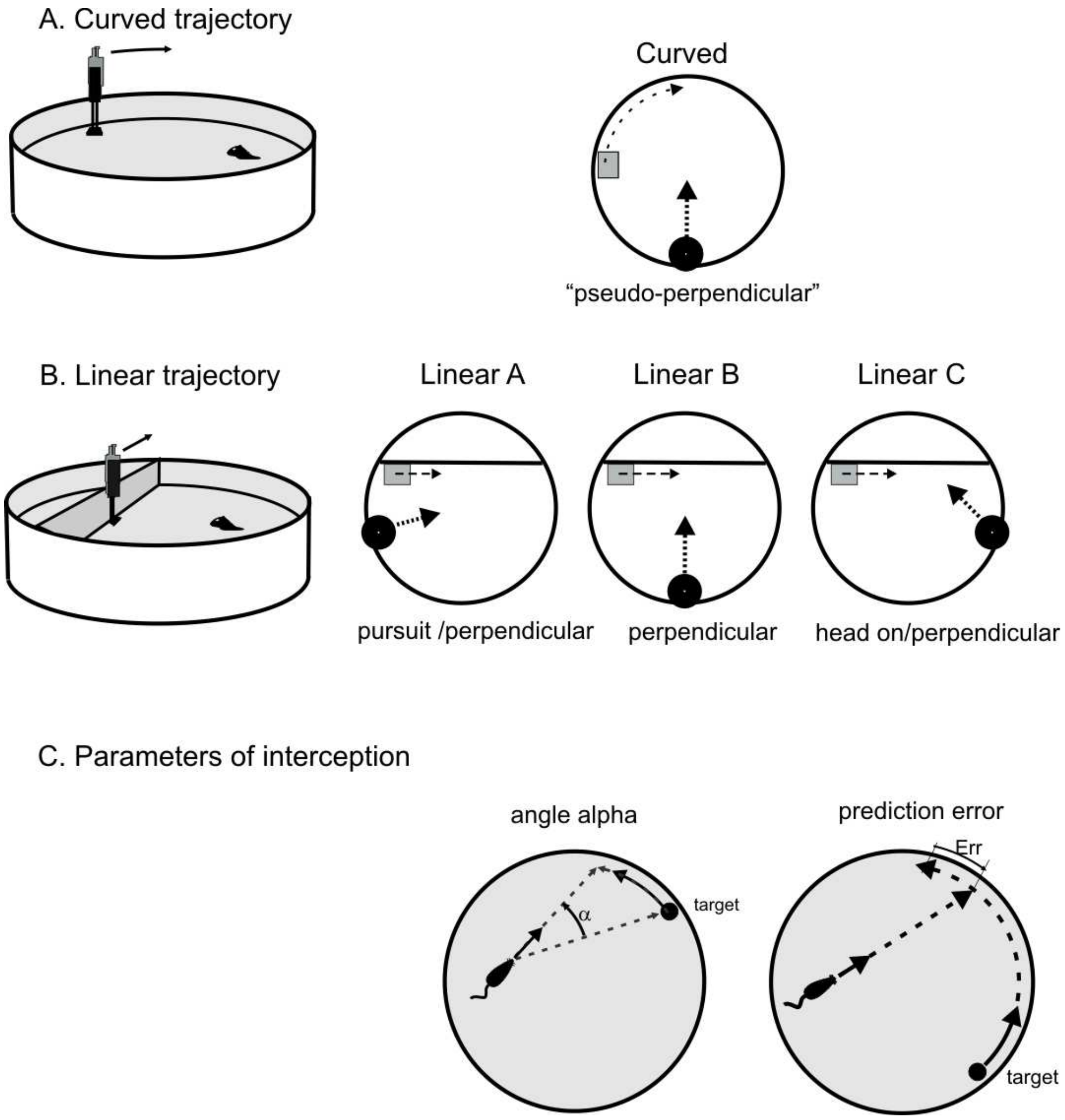


Figure 2.4.2: *A: Left- Scheme of experimental design. Rat navigated toward a moving robot with platform moving along a curved trajectory at the water maze wall. Right - Configuration between the starting positions of the rat and the target. B: Left - Scheme of experimental design, in which rats navigated toward a goal moving along a straight trajectory. Right - Configuration between the starting positions of the rat and the target. C: Parameters used for analysis. Left - angle* α *Rigth - Prediction Error.*

movement. In each navigation session we controlled both starting position of the rat and starting position of the target relatively to each other and with respect to the room frame (see Fig. 2.4.2 A-B). The target and the rat were given in each session pseudorandomly for their start positions and particular blocks. The speed of the target was always lower than the maximal speed of the rat . We changed target speed pseudorandomly between sessions but it remained constant during the sessions. Training procedure consisted of a two day pretraining part in which animals learned to navigate toward the stable and very slowly moving platform. Since the day three rats were trained to navigate toward a moving target.

Data analysis

The sessions were recorded on a DVD-recorder with a sampling rate of 25 frames per second. MatLab functions written by the authors were used to extract trajectories of both a rat and the target and to process them. We tracked two points on the rat (center of gravity and tip of rat's nose) and one point on the target (center of gravity). The trajectories were smoothed with a 5-point running mean. Velocity vector was calculated from the smooth trajectories as difference between two positions recorded 400 ms apart divided by the duration of this interval. From the velocity vector we calculated speed and heading direction of the rat and of the target. Rat's speed was calculated from the trajectory of the center of gravity. This ensured that the speed was small when the rat rotated on a place. All the other variables were calculated from the trajectory of the rat's nose. The reason for this was that the nose trajectory was easier to interpret than the trajectory of the center of gravity. The rats made contact with the target with front parts. In addition they were able to quickly change movement of their front parts while their bodies tended to continue in the previous direction. As the result the intended changes in heading direction were first visible in the nose trajectory and with a delay and less clearly in the body trajectory.

In this follow up study we had focused on selected parameters of interception. For analysis we calculated oriented angle α, which is an oriented angle between rat's heading direction and the rat-to-target direction Fig.2.4.2C. Angle α is positive if the rat swims ahead of the target movement (up to 180°). Next parameter prediction error- Err reflect rat actual estimate of a place of contact with the target. If value of Err is zero, animals navigate toward the future place of contact with the target.

Part IV

Results

2.5 Inertial stimuli in the carousel arena

Text of results were adapted from original manuscript of Blahna et. al (2011)

In Phase 1 the two groups of rats, A (n=7) and B (n= 7), were trained in the standard and modified active avoidance task, respectively. In Phase 2 the two tasks were swapped between the groups.

2.5.1 Phase 1

The to-be-avoided sector was on the South (180) during Phase 1. Six rats trained in the standard active place avoidance task (Group A) learned the task within six sessions (Figure2.5.1, Sessions 1-6). Only one rat (rat #12) performed considerably worse than the other rats (Fig.2.5.1, Sessions 1-6). Its performance improved slower. On the contrary, six out of seven rats trained in the modified active place avoidance task (Group B) did not improve during these six sessions (Figure2.5.1, Sessions 1-6). One rat from Group B (rat #8) learned the task equally well as the rats from Group A (Fig. 2.5.1, Sessions 1-6). We compared performance of both groups in the beginning of the training (Session 1) and after reaching stable level of performance (Session 6) by two-way ANOVA with “group" as between subject factor and “session" as within subject factor. Since the performance in the active place avoidance task is commonly assessed by four variables (see section Data analysis in Material and Methods), we ran four separate statistical tests. Two variables, *number of entrances into the to-be-avoided sector*" and *maximum time spend outside the to-be-avoided sector*; reflect cognitive abilities of the subject. The third variable, *time to the first entrance into the to-be-avoided sector*, also reflects cognitive abilities of the subject plus its long-term memory for the location of the to-be-avoided sector acquired in the previous sessions. The fourth variable, *path length*, reflects locomotor activity of the subject. The groups differed in the number of entrances (F(1,12) = 13.01, p = 0.0036), in the maximum time avoidance (F(1,12) = 15.32, p = 0.0021) and in the time to the first entrance (F(1,12) = 14.20, p = 0.0027) but not in the path length (F(1,12) = 1.32, p = 0.2727). Session 1 differed from Session 6 in the number of entrances (F(1,12) = 22.81, p = 0.0005), in the maximum time avoidance (F(1,12) = 25.40, p = 0.0003) and in the time to the first entrance (F(1,12) = 16.51, p = 0.0016) but not in the path length (F(1,12) = 0.03, p = 0.8623). Figure 2.5.1 indicates that the differences between Session 1 and Session 6 are due to the improvement of Group A as the performance of Group B did not change. This is also reflected in the interaction of the factors "group" and "session". The interaction was significant for the number of entrances (F(1,12) = 12.40, p = 0.0042) and for the maximum time avoidance (F(1,12) = 7.96, p = 0.0154) but not for the time to the first entrance (F(1,12) = 1.06, p = 0.3232) and for the path length (F(1,12) = 0.44, p = 0.5180). Subject's position on the arena can be expressed in polar coordinate system with origin in the center of the arena and with zero angle in the center of the to-be-avoided sector. The angular component of this polar representation (see angle ϕ in Figure 1B) expresses subject's position with respect to the to-be-avoided sector. A plot of the angle ϕ as a function of time brings a detail view on subject's behavior during a session (Figures 2.5.2 and 2.5.3 - aversive stimuli are denoted by black dots) (Fajnerova, Kenney, Klement, unpublished data). When a rat is sitting, the angle ϕ is decreasing at a constant rate (see the reference slope in Figures 2.5.2 and 2.5.3). If the rat is moving in the direction of arena rotation the angleϕ is decreasing at faster rate. If the rat is moving against arena rotation faster, at the same speed or slower than the arena rotates then the angle ϕ is increasing, constant or decreasing at slower rate than the reference slope. The radial component of the polar coordinate system is less important for describing subjects' behavior during sessions. Most of the time rats are close to the arena wall. For example, the rats in the present experiment spent 80% of time near the arena wall (up to 11.5 cm from the arena wall) and only 20% in the central part of the arena (up to 28 cm from the center of the arena) which covered the same area as the 11.5 cm wide annulus along the wall. In addition, moving towards or away of the center of the arena does not help the subject to avoid the to-be-avoided sector. Figure 2.5.2 shows behavior of a typical rat (rat #1) in the standard active place avoidance task in the beginning of the training

(Session 1) and after reaching the stable level of performance (Session 6). In the beginning of Session 1, the rat moved rather chaotically. Later, it responded to the aversive stimulus by short runs either in the direction or against the direction of the arena rotation. Otherwise the rat was sitting. In Session 6, the rat avoided the to-be-avoided sector well. It alternated sitting with short runs against the direction of the arena rotation. The runs, avoidance reactions, had been initiated before the rat received aversive stimuli. The runs were short enough such the rat did not enter into the to-be-avoided sector from the other side. Rat #8 from Group B which learned the modified active place avoidance task behaved similarly to this rat. Figure 2.5.3 shows behavior of a typical rat (rat #11) in the modified active place avoidance task. The behavior is shown in the beginning of the training (Session 1) and in the end of the training (Session 6). The rat was sitting most of the time, especially at the end of Session 6. It responded to the aversive stimuli by short runs in the direction of the arena rotation.

2.5.2 Phase 2

One rat from Group B (rat #8) learned the modified active place avoidance task. It indicated that rats can solve this task even though only small number of them is able to learn an effective strategy. We tested whether mastering the standard task can help to solve the modified task. Therefore we swapped the two tasks between the groups. In addition, we changed the location of the to-be-avoided sector from South (180) to North-Northeast (22.5). The rats which mastered the standard active place avoidance task in Phase 1 (Group A without rat 12) quickly learned the modified task (Fig 2.5.2, Sessions 7-10). Their performance decreased in the first session after the change (Session 7) but it returned to the pre-change values in the next session (Session 8). Rat 12 improved its performance at the end of the training (Fig. 2.5.2, Sessions 7-12). We compared the performance of the rats from Group A across Session 6, 7 and 8 by one-way ANOVA with “session” as repeated measures. Tukey’s post- hoc test was used for multiple comparisons. The four evaluated variables were transformed as in Phase 1. The number of entrances differed across the sessions (F(2,12) = 23.77, $p = 0.0001$, Session 7 > Session 6 = Session 8) as well as the maximum time avoidance (F(2,12) = 8.64, $p = 0.0047$, Session 7 < Session 6 = Session 8) and the time to the first entrance (F(2,12) = 29.58, $p < 0.0001$, Session 7 < Session 8 < Session 6). The path length was not different across the sessions (F(2,12) = 0.46, $p = 0.6421$). Figure 2.5.2 shows behavior of rat #1 at the end of training in the modified active place avoidance task (Session 10). The rat used the same strategy as in the standard task (Session 6). We also tested whether the rats from Group B learn the standard active place avoidance task after they have been trained in the modified task. The rats which did not learn the modified task in Phase 1 (Group B without rat #8) performed badly also in the standard task (Fig2.5.1 Sessions 7-12). The rat 8 which learned the modified task in Phase 1 performed well also in the standard task (Figure 2.5.1, Sessions 7-10). In order to see a possible improvement of Group B in Phase 2, we excluded rat #8 from statistical tests. This rat clearly mastered both tasks and it cannot further improve. Thus we compared the performance of the rats from Group B without rat #8 across Session 6, 7 and 12 by one-way ANOVA with "session" as repeated measures. Tukey's post-hoc test was used for multiple comparisons. The number of entrances did not differ across the sessions (F(2,10) = 3.279, $p = 0.0803$) as well as the maximum time avoidance (F(2,10) = 3.8349 $p = 0.0581$). There were differences in the time to the first entrance (F(2,10) = 17.90985, $p = 0.001$), Session 6 < Session 7 < Session 12). The path length was not different across the sessions (F(2,12) = 2.165, $p = 0.1654$). The rats from Group B did not improve, except they increased the time to the first entrance into the to-be-avoided sector. This increase, at least partially, reflects non-specific changes in behavior due to the arena rotation because the time to the first entrance increased between Session 6 and 7. The location of the to-be-avoided sector in Session 7 was different from the location of the to-be-avoided sector in Session 6, therefore, the rats did not know the location until they entered into the sector. The time to the first entrance was longest in the last session (Session 12), however, it was still shorter than the time to the first entrance in Group A in the same task after the same amount of training (Session 6) (t-test: $t11 = 2.4567$, $p = 0.03187$). Despite the statistical tests did not show larger improvement, the detail view on the time course of angular position of these rats (see angle ϕ in Fig. 2.1.1 B) in the last session in Phase 2 (Session 12) indicates that some rats learned the location of the to-be-avoided sector, however, they did not know how to avoid it. Rat #11 is an example. In Figure 2.5.3 (Session 12) are periods in which rat #11 alternated sitting with short runs against arena rotation similarly to the efficient solvers of the task, however, there are also periods in which the rat alternated sitting with short runs in the direction of arena rotation. Both types of runs were mostly initiated before the rat was brought into the to-be-avoided sector. When running through the to-be-avoided sector, the rat was not fast enough to pass the sector in less than 0.5 s in order to avoid aversive stimulus. The initiation of avoidance reaction before the to-be-avoided sector indicates that the rat knew the location of the to-be-avoided sector but it was not able to avoid the sector effectively. Some rats from Group B did not search for the effective strategy during Phase 2. They were sitting on the arena during the whole session.

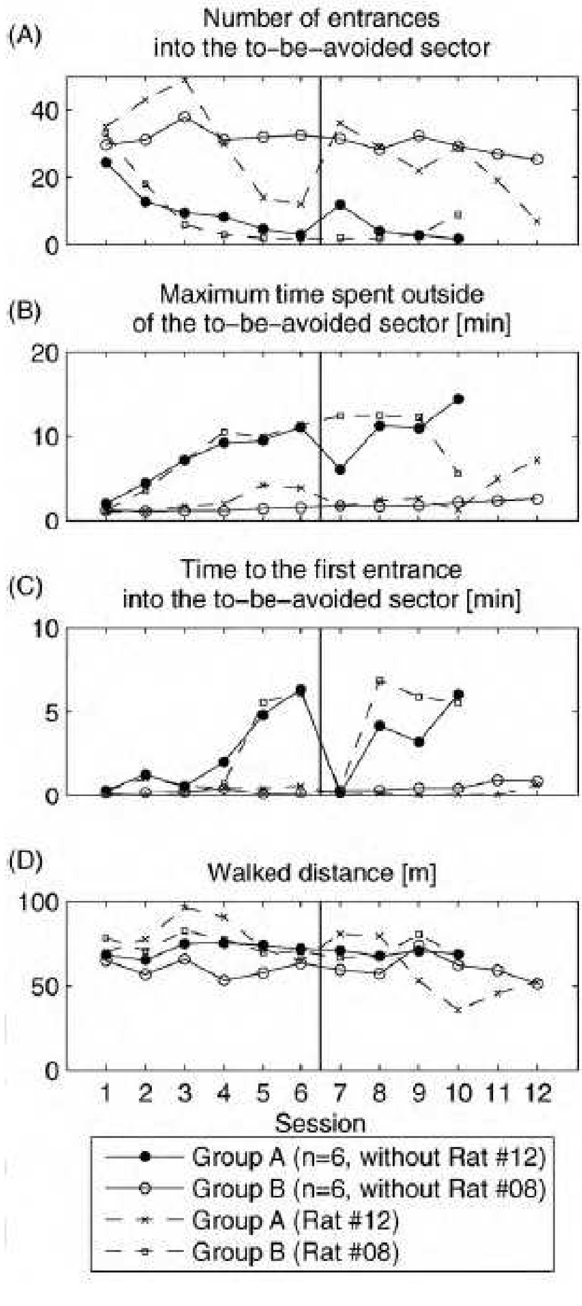


Figure 2.5.1: *Performance of the rats trained in the standard active place avoidance task (Group A: Sessions 1-6; Group B: Sessions 7-12) and in the modified active place avoidance task (Group A: Sessions 7-12; Group B: Sessions 1-6). The vertical lines indicate the time when the two tasks were swapped between the groups. A. Average number of entrances into the to-be-avoided sector. B. Average maximum time spent outside the to-be-avoided sector. C. Average time to the first entrance into the to-be-avoided sector. D. Average path length (Adapted from Blahna et al. 2011).*

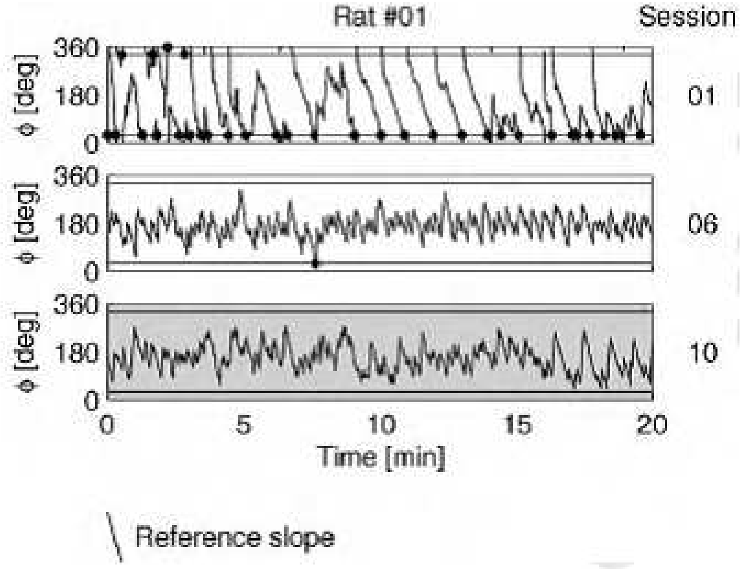


Figure 2.5.2: *Behavior of a typical rat in the beginning and in the end of the training in the standard active place avoidance task (Sessions 1 and 6) and in the end of the training in the modified task (Session 10). The graph shows the time course of angular distance between the rat and the center of the to-be-avoided sector (see angle ϕ in Figure2.1.1B). Shocks are denoted by black dots. Reference slope shows the time course of phi for a non-moving object passively transported by the arena (Adapted from Blahna et al. 2011).*

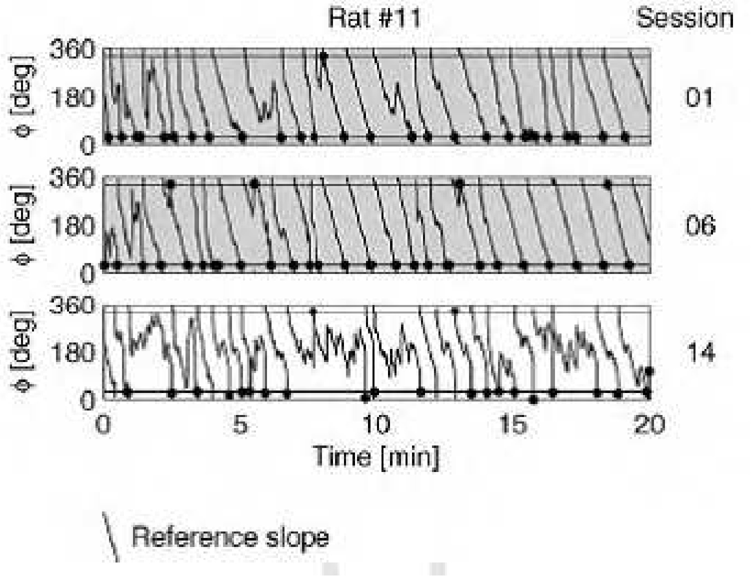


Figure 2.5.3: *Behavior of a typical rat in the beginning and in the end of the training in the modified active place avoidance task (Sessions 1 and 6) and in the end of the training in the standard task (Session 14). The graph shows the time course of angular distance between the rat and the center of the to-be-avoided sector (see angle ϕ in Fig. 2.1.1). Shocks are denoted by black dots. Reference slope shows the time course of ϕ for a non-moving object passively transported by the arena (Adapted from Blahna et al. 2011).*

2.6 Role of the posterior parietal cortex

Text of the main results was adopted from the original paper of Svoboda et al. (2008). Whole manuscript is attached in this thesis.

2.6.1 Arena-defined to-be-avoided sector

Number of entrances best characterized the learning process. Analysis of the task performance showed that both groups Lesioned and Sham controls improved across sessions as assessed by the number of entrances (A two-way ANOVA (LESION×SESSIONS) showed a significant main effect of SESSIONS (F (4,68) = 9.77; P $<$ 0.001) but failed to show an effect of LESION (F (1,17) = 0.384; P = 0.54). No interaction between the two factors was found (F (4,68) = 0.321; P = 0.86). These results suggest that both groups improved similarly during training and showed similar avoidance performance once the task was acquired (see Fig. 2.6.1).

2.6.2 Room-defined to-be-avoided sector

Both groups of animals improved their learning in avoidance of the room defined to-be-avoided sector. Analysis of number of entrances decreased during sessions for both groups of animals (See Fig. 2.6.1). Two-way ANOVA (LESION×SESSIONS) failed to reveal a significant main effect of LESION (F (1,17) = 1.16; P = 0.3), but it showed a significant effect of SESSIONS (F (4,68) = 12.15; P $<$ 0.001). No interaction between those two factors was found (F (4,68) = 0.46; P = 0.77).

2.7 Enemy avoidance

Text of results was adapted from the original manuscript which was submitted by Telensky et al.. into the PNAS.

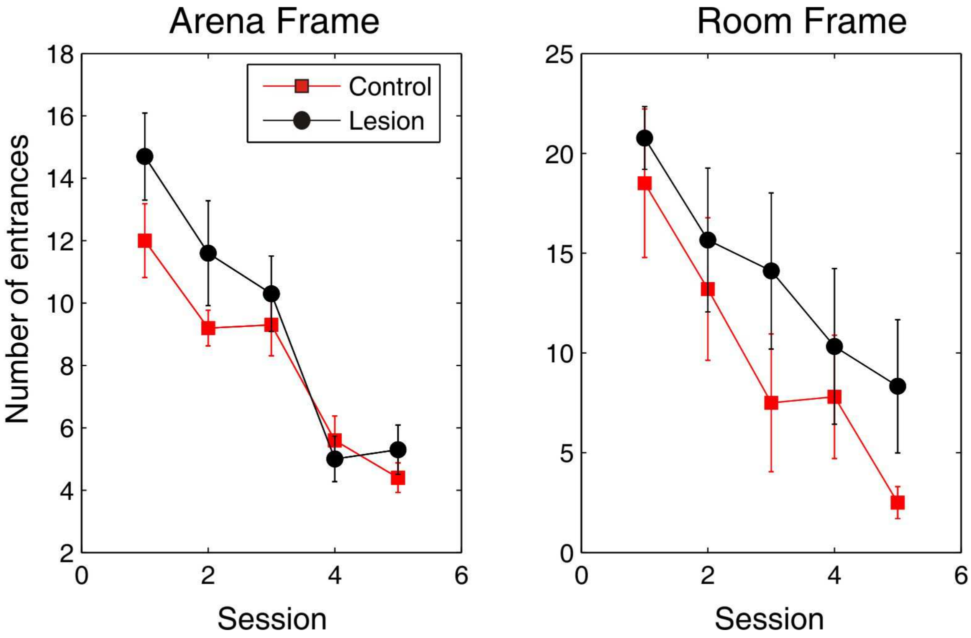


Figure 2.6.1: *Number of entrances into the to-be-avoided sector in rats with lesion of the parietal cortex (Lesion) and Sham operated control animals (Control). Left: Performance of animals trained to avoid arena frame defined to-be-avoided sector. Right: Performance of animals trained to avoid room frame defined to-be-avoided sector. Adapted from Svoboda et al. (2008).*

2.7.1 Avoidance of a conspecific

The animals rapidly learned to collect the food pellets dropped on an arena floor during the 14-day pretraining phase. Once this phase had been completed, rats from both groups displayed intensive foraging behavior. On the final day of this pretraining, rats from the Subject group traveled a mean distance of 82.1±9.8 m (mean±S.E.M.). Animals from the Enemy group walked 95.2±3.4 m. There were no between-group differences as revealed by a two sample t-test (t(8) = 1.86; P > 0.05). During the pretraining phase, animals from both groups displayed a slight preference for the central part of the arena compared to the periphery. The periphery dwelling on the last day of pretraining was 27.9±1.8% in the rats from the Subject group, and 23.7±1.5% in the animals from the Enemy group. A two-sample t-test revealed no differences between groups (t(8) = 1.86; P > 0.05). Upon introducing negative reinforcement to subject rats in the first training session, the animals in the Subject group showed a clear tendency for thigmotaxis and decreased locomotion. Periphery dwelling of the Subject group rapidly increased to 64.2±2.8% (paired t(4) = 2.78; $P < 0.001$ – between last day of pretraining and initial day of training), accompanied by significant decline of total distance to 37.1±7.5 m (paired t(4) = 3.97; $P < 0.02$). This contributed to the decrease in the number of entrances into the 25 cm distance from the Enemy animal, which had dropped from 136.6±0.6 on the last day of pretraining to 64.4±1.3 on the first day of training (paired t (4) = 2.78; $P < 0.001$). During the consequent training period, the number of entrances into the punishment area further decreased (ANOVA, F(15,60) = 20.58; $P < 0.001$), reaching the asymptote of approximately 15 entrances on the 9th training session (measured by an absence of between session improvement; Newman–Keuls post hoc test; $P > 0.05$). The training-induced decrease of number of errors is shown in Fig.2.6.1 Whereas periphery dwelling in subjects rats remained unchanged during the training period (ANOVA, F(15,30) = 1.58; $P = 0.11$), the elapsed distance in the Subject group dropped (ANOVA, F(15, 60) = 24.44; $P < 0.0001$). We have also evaluated the contribution of either rat in the pair to approaching each other by calculating the fraction of path elapsed during 3-s intervals immediately preceding the first footshock resulting from the given error. In all enemy-subject pairs, the enemy rats walked significantly longer distances during those intervals (see Fig. 2.7.2 A), which shows that these errors may have been caused by natural agonistic activity of enemy rats instead of the active approaching of subject rats. To demonstrate whether the decrease in the number of entrances during the course of training is fully attributable to the decreasing locomotor activity, or whether the animals succeeded in improving their behavioral strategy in order to avoid the enemy more efficiently, we measured the path elapsed between two entrances into the shock zone. Fig.2.7.2 B shows the natural logarithm of the average path walked between two consequent entrances for all training sessions. This value significantly increased during training (ANOVA, F(15,60) = 5.021; $P < 0.0001$) which suggests that other changes took place in behavior of the subject rats other than lowered locomotion and increased thigmotaxis.

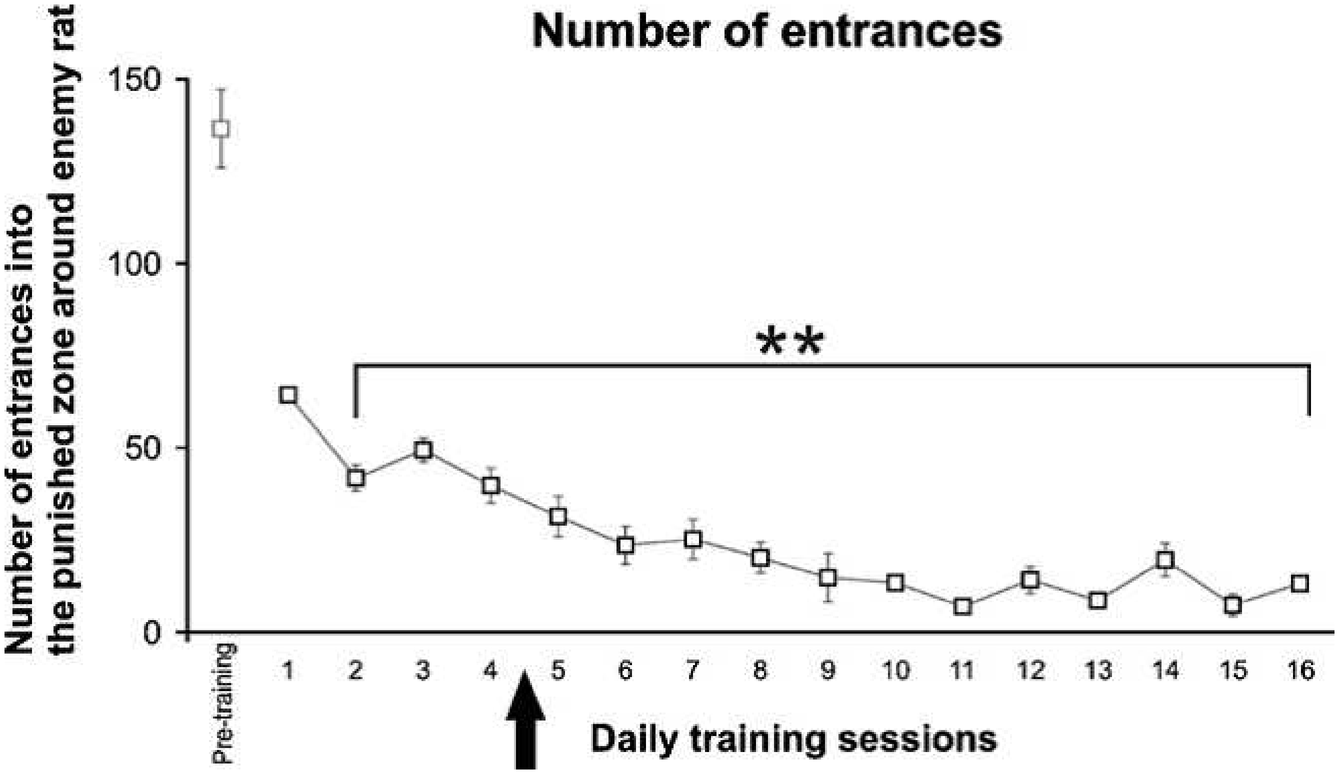


Figure 2.7.1: *Number of entrances into the 25 cm zone of the enemy rat, during last pre-training session and 16 training sessions (mean±S.E.M.). Entrances into this zone were punished by mild footshocks during the acquisition sessions (1–16). The arrow denotes when four auxiliary sessions (performance not shown) were added to facilitate the acquisition process. Upon finishing auxiliary sessions the number of entrances rapidly decayed until session 9 when it approximately reached the asymptotic value (see Section 3 for details). Two asterisks denote significant decrease in the number of entrances compared to the initial day of training ($P < 0.01$) (Adapted from Telensky et al., submitted).*

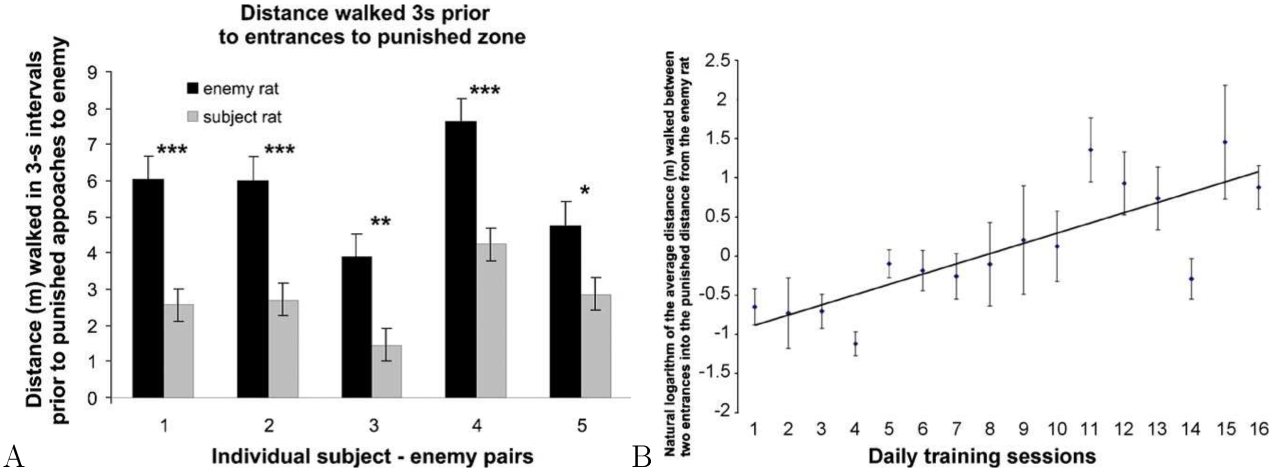


Figure 2.7.2: _A: Distance (mean±S.E.M.) walked during 3- s time intervals immediately preceding punished entrances into the prohibited area during a session (average for all training sessions). In all pairs, enemy rats walked significantly more during these intervals (stars denote probability levels obtained by Newman–Keuls post hoc test: ***$P < 0.0005$; **$P < 0.005$; *$P < 0.05$). Most entrances of the subject rat into the punishment area thus resulted not fromavoiding the enemy rat but rather approaching it. B:Natural logarithm (ln) of average path (mean±S.E.M.) walked by the subject rats between two consequent entrances into the punishment 25 cm zone of the "enemy" rat. Increase in this measurement during the course of learning suggests that the subject rats improved their avoidance behavior over time (adapted from Telensky et al., submitted)._

2.7.2 Avoidance of a robot

Effect of hippocampal inactivation on Enemy Avoidance

Rats learned to avoid the moving robot (M group) over the 6 days of training. Inactivating the hippocampus by TTX on day 7 abolished the avoidance (Fig.2.7.3 A). In contrast, the vehicle infusion on day 8 did not affect the avoidance. The one-way ANOVA on the number of shocks found a significant effect of days (F7, 49= 7.74, p<10-5). The post-hoc tests showed that the avoidance was asymptotic from day 3 (day 1 > days 3-6 & day 8 - saline session) and that on day 7 (TTX), the performance was reduced to the level of day 1 (significantly worse than all other sessions). Similarly, rats learned to avoid a stable robot well (S group; F7,56 = 2.30, p<0.05; Fig. 2.7.3 B). However, in this case, the inactivation had no effect on the avoidance. The post-hoc test showed that the number of footshocks decreased over days (day 1 > days 2, 5 & 6) and neither the TTX infusion on day 7, nor the saline infusion on day 8 had any effect on the avoidance. The lower absolute value of shocks in the S group on day 1 indicates that avoiding the moving robot was more difficult than avoiding the stable robot.

Effect of hippocampal inactivation on locomotion

Locomotion patterns varied during the course of the experiment. The one-way ANOVA on the total path traveled during a session found a significant effect of days in the M group (F7, 49 = 2.29, p<0.05; Fig.2.7.4 A). The post-hoc tests showed that rats walked less on days 5 and 7 compared to day 1 (both p's<0.05), but not relative to day 8 (vehicle infusions). The one-way ANOVA also found a significant effect of days on thigmotaxis in the M group (F7, 49 = 2.28, p<0.05), but the post-hoc tests failed to find significant differences between any two sessions. In the S group, the one-way ANOVA found no effect of days on the total path (F7,56 = 1.81, p>0.05; Fig. 2.7.4 B), but it found a significant effect of days on thigmotaxis (F7,56 = 2.99, p<0.01]. The post-hoc test found that thigmotaxis was reduced in the TTX session on day 7 compared to all other sessions

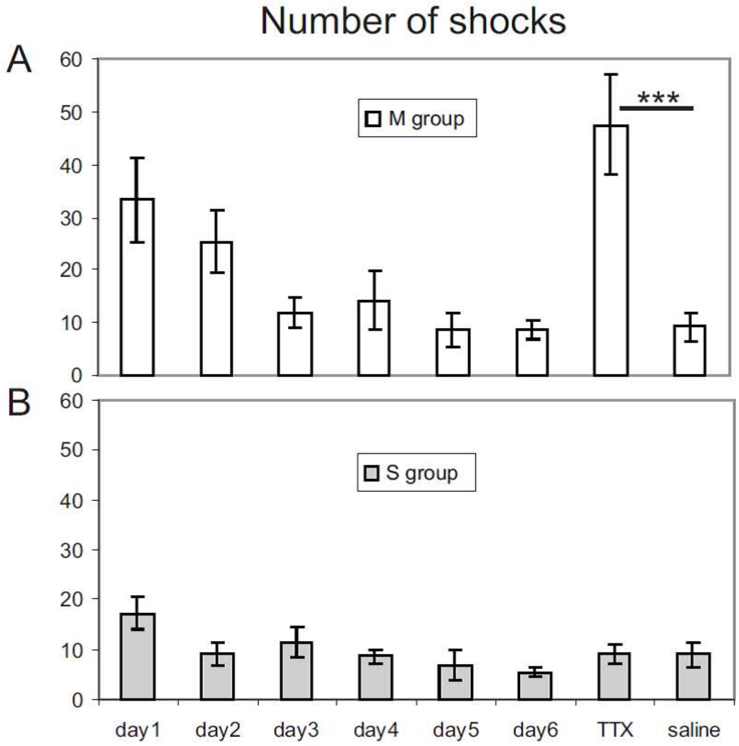


Figure 2.7.3: *The effect of hippocampal inactivation on Enemy Avoidance (shown as the average number of shocks ± S.E.M.). Panel A. Avoidance of a moving robot (M group). Bilateral inactivation of the dorsal hippocampus by infusion of TTX on day 7 significantly increased the number of shocks received as a result of the robot approaches compared to vehicle infusions on day 8, (***, $p<0.00001$). Panel B. Avoidance of a stable robot (S group). The robot was turned off in this version of the task, but it was moved to a different position by the experimenter in the middle of each training session. In this case, hippocampal inactivation had no effect on the avoidance (Adapted from Telensky et al., submitted)*

(all ps$<$0.05). This suggests that hippocampal inactivation partially alleviated the border-escaping response to a stressful stimulus. However, this effect was non-significant when avoiding a moving robot.

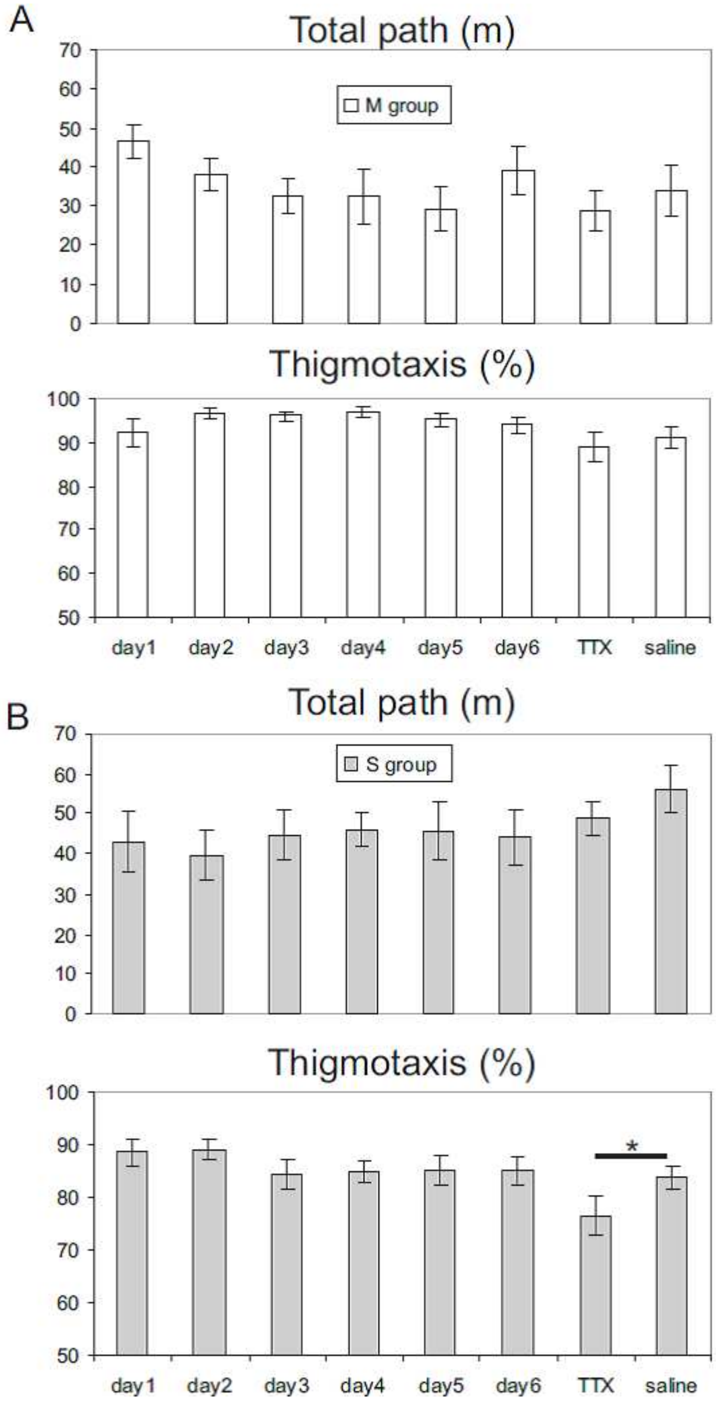


Figure 2.7.4: *The effect of hippocampal inactivation on locomotor behavior shown as the average total path length [m ± S.E.M.] and average level of thigmotaxis [% ± S.E.M.]. Panel A. Avoidance of a moving robot (group M). Hippocampal inactivation by TTX on day 7 did not significantly alter the overall locomotion or thigmotaxis compared to vehicle infusion on day 8. Panel B. Avoidance of a stable robot (S group). Hippocampal inactivation by TTX on day 7 did not influence the overall locomotion. The level of thigmotaxis was moderately, but significantly, decreased (i.e. the animals tended to spend more time in the central part of the arena) after the TTX infusion compared to the vehicle infusion on day 8 (*, $p<0.05$) (Telensky et al., submitted).*

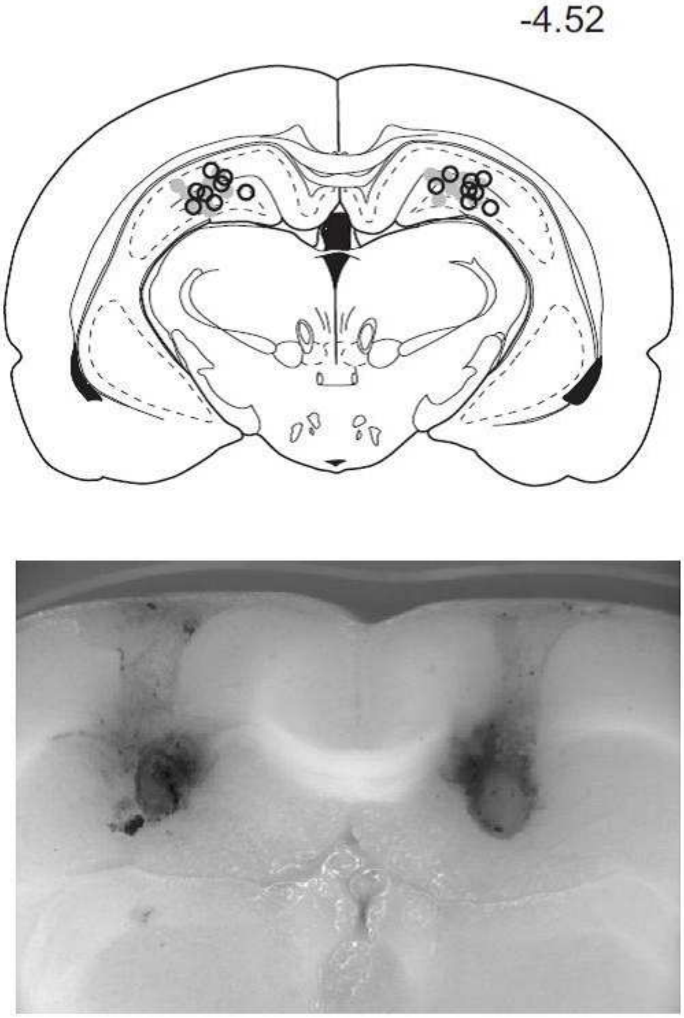


Figure 2.7.5: *Histological control of the infusion site placement in the hippocampus. Top: End of tracks of infusion cannulae (M group - black circles, S group - grey circles) were verified post mortem on coronal brain sections (adapted from Paxinos and Watson, 33). Bottom: Image of a representative brain slice. The extent of the tissue affected by the TTX infusion was estimated using infusions of black ink in the same volume as the TTX infusions. The ink blots showed no signs of excessive extrahippocampal leakage (Telensky et al., submitted).*

2.8 Rat interception behavior

2.8.1 Pilot study

We present behavior of rats (n = 7) trained to swim toward a moving target. It is 53 sessions (7-8 sessions per rat) in which the target moved slower than the rats (slow sessions) and 39 sessions (5-6 sessions per rat) in which the target moved faster than the rats (fast sessions).

Slow sessions

In the slow sessions average speed of the target was between 9 and 24 cm/s. The rats increased their swimming speed at the beginning of the session. We considered the moment of the acceleration as the beginning of a navigational attempt. According to this criterion the rats started navigation 2.2 s to 5.1 s (average 3.3 s) before they caught the target. During the last second they swam with speed 41,4 cm/s. Fig. 2.8.1 shows navigational trajectories of 3 rats. The onset of the acceleration cannot be seen in all the examples in Fig. 2.8.1 (2nd column). Sometimes the rats increased their speed when experimenter holding the target was coming to the pool. It was before the digitalization started. The trajectories are either curved-targetwise (Fig. 2.8.1, odd rows) or straight (Fig.2.8.1, even rows). Thirty eight (72%) of the trajectories were curved and 15 (28%) were straight. In individual rats the numbers of the curved-straight trajectories were: 6-2, 3-4, 8-0, 5- 3, 4-3 5-3 and 7-0. We classified the trajectories subjectively. Except 3 trajectories the classification was clear. One of the “problematic" trajectories is shown in Fig.2.8.1 (Rat 7 - straight trajectory). The rat did not swim straight to the place of contact but along an S-shape path. Despite of it this trajectory has some common features with the other straight trajectories.

The straight trajectories are characterized byα greater than zero; its time course becomes approximately constant after the subject has adjusted its heading direction. The same is true for the time courses of β and γ. The prediction error (Err) becomes small shortly after the beginning of navigation. The curved trajectories have α equal to or smaller than zero and their time course

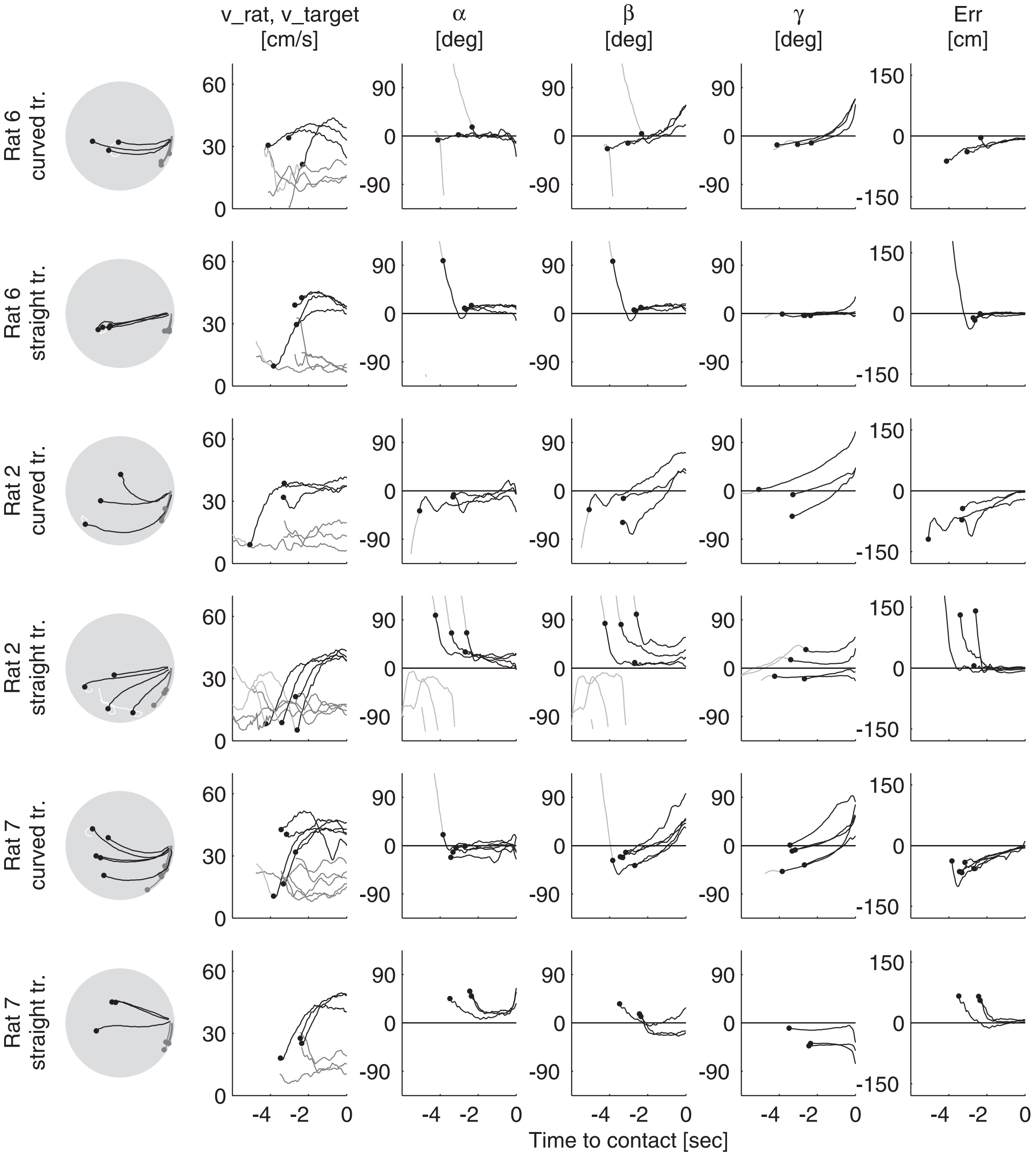


Figure 2.8.1: *Trajectories and time courses of v (speed),* α, β, γ *and Err of three representative rats recorded in the slow sessions. The trajectories in the 1st column are transformed in such a way that the target moves counter-clockwise and the subject reaches it on East. The trajectories are divided according to their shape into curve and straight. Beginnings of navigation are indicated by filled circles. Rats' behavior before this moment is shown as the white lines in the 1-st column and as the light gray lines in the other columns. Rat's behavior during navigation is depicted by the black lines. Target trajectory (1-st column) and its speed (2-nd column) are shown as the gray lines (Adapted from manuscript Klement and Blahna, unpublished data).*

is also approximately constant. The time courses of β and γ are increasing and the prediction error (Err) is negative. The fast changes of β and γ at the end of navigation in Fig. 2.8.1 are due to inaccuracy of estimation of these parameters rather than due to behavior of the subjects. The estimation is biased if the animal does not swim toward the center of the target but toward its edges. The error increases with decreasing distance between the animal and the target. We fitted the time courses of α,β and γ during the interval 0.8 s after the onset of navigation up to 0.2 s before the contact by linear functions. We did not fit the first 0.8 s of navigation because the rats were adjusting their heading direction and the last 0.2 s because of the increasing error in the estimation of α and γ. We denoted this interval as *I*. For the curved trajectories, was -0.3 ± 1.4° in the middle of the interval *I*, which corresponds to the average value of α during *I*, and its slope was 4.0±0.8°/s. The average value of α was not different from zero (one-sample t-test: t_{36} =-0.21, P = 0.83) while the increased was significant (one sample t-test: $t_{36} = 5.30$, $P < 10^{-5}$). The oriented angles β and γ increased as well with rates 20.6±1.3°/s, 16.7 ±1.2°/s, respectively (one sample t-test: β: $t_{36} = 16.16$, $P < 10^{-17}$; γ: $t_{36} = 14.16$, $P < 10^{-15}$).

For the straight trajectories, the average value of α was 15.7°±1.3. This was significantly greater than zero (one sample t-test: $t_{15}= 11.95$, $P < 10^{-8}$). The oriented angles α,β and γ were approximately constant. The slopes of linear functions fitted on the time courses of these angles were -0.4 ±1.2°/s for α, 1.4 ±0.9 s for β and 1.9±1.0°/s for γ . None of the slopes was different from zero (one sample t-tests: α: t_{15} = -0.37, P = 0.72, β : $t_{15} = 1.54$, P = 0.14, γ: $t_{15} = 1.84$, P = 0.09, respectively). Figure2.8.1 shows all the recorded trajectories divided into the curved and straight types. dα soon becomes small in both types of trajectories indicating that the rats might null changes of α during navigation. The other parameters differ between the groups. For the curved trajectories, dβ and dγ are positive and Err is initially negative and increases to zero. For the straight trajectories all the parameters soon become approximately zero.

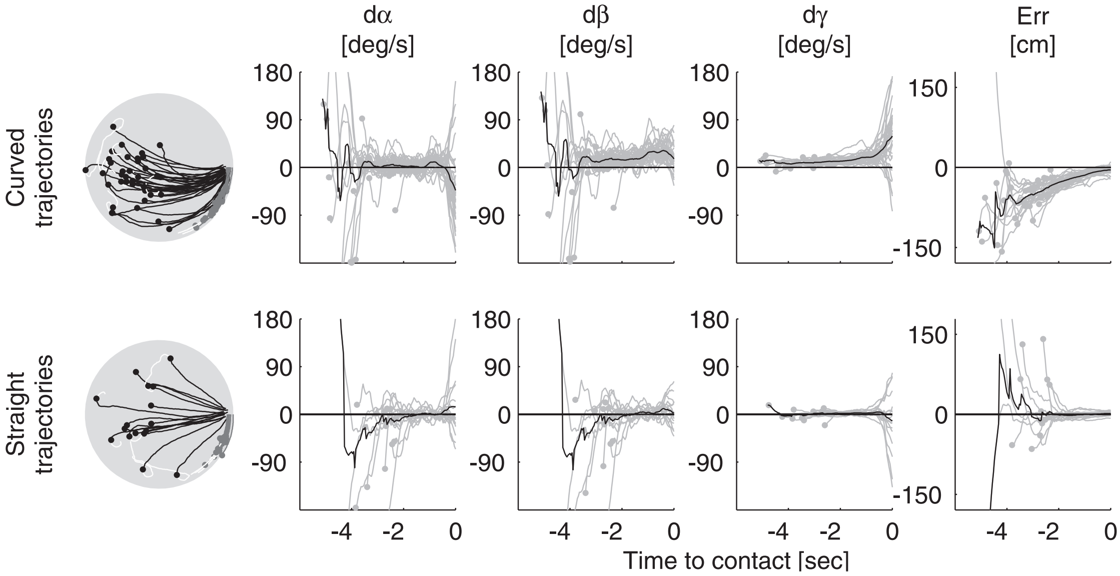


Figure 2.8.2: *Trajectories and time courses of* $d\alpha$*,* $d\beta$*,*$d\gamma$ *and Err from all the slow sessions. The trajectories in the 1-st column are transformed in such a way that the target moves counter-clockwise and the subject reaches it on East. The trajectories are divided according to their shape into curved and straight. Beginnings of navigation are indicated by filled circles. Rats' trajectories before this moment are shown in white color in the 1-st column. The columns 2 to 5 shows the average time course of the corresponding parameter as the black line and the time course of individual navigational trials as the gray lines (Adapted from manuscript Klement and Blahna, unpublished data).*

Fast sessions

In the fast sessions average speed of the target ranged between 53 and 65 cm/s. Usually the rats did not catch the target when they attempted to do so. Thus the fast sessions consisted of periods, trials, when the subject navigated toward the target interspersed by other kinds of behavior. Figure 2.8.3 shows a rat which tried to reach the target 8 times before it succeeded. During the trials the rat kept the oriented angle between 15° and 75° (see shaded areas in Fig. 2.8.3, 2nd row). The trials started with speed acceleration (Fig. 2.8.3, 3rd row). The speed remained high until the rat either reached or missed the target.

As in the slow sessions we used rat speed to define the beginnings of the trials. The beginning of a trial was the moment of acceleration followed by target-directed movement. Since we were not able to unambiguously interpret behavior of the rats following each of the accelerations, we analyzed the successful trials only. The rats markedly corrected their heading direction during some trials. It resulted in a temporary decrease of speed followed by another acceleration. In this situation two or even more possible beginnings of the trial could be used. We choose the earliest acceleration after which the subject swam toward the target or ahead of target's movement until the end of session (α remained within -15° and 150°).

According to this definition the successful trials lasted from 1.4 s to 5.3 s (average: 3.3 s). During the last second the rats swam with speed 38.5 cm/s. Figure2.8.4 shows behavior of three rats during the last 6 seconds. The moment of acceleration is clearly visible. The trajectories of Rat 7 are divided into two groups - curved (Fig.2.8.4, 1st row) and tortuous (Fig. 2.8.4, 2nd row). The curved trajectories resemble the curved trajectories in the slow sessions. They are bent targetwise and the prediction error (Err) is negative. Unlike in the slow sessions is positive however this was necessary condition for reaching the fast-moving target. The tortuous trajectories are closer to the center of the maze than the smooth trajectories. This was also true for the tortuous trajectories observed in other rats. The tortuosity is present in the beginning. In the end the trajectories are smooth. Thus they consist of two parts. The moment of switch is visible in the speed profile

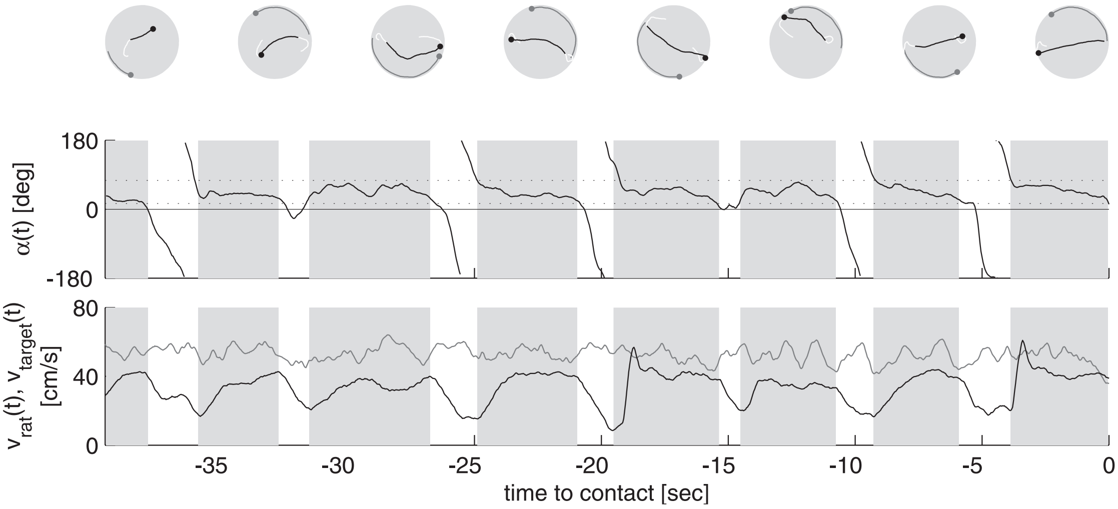


Figure 2.8.3: *Behavior of one of the rats during a fast session. The rat attempted to reach the target several times before it succeded. The attempts are indicated by the gray color in the time courses of* α *(2nd row) and speed (3rd row). Rat's trajectories and target's trajectories during the attempts are shown in the first row as black and gray lines respectively. The beginnings of the navigation are indicated by the filled circles. The white lines in the first row denote rat's trajectories 1 second before and 1 second after the attempts. The two dotted lines in the time course of* α *(2nd row) indicate 15°and 75°. In the 3rd row momentary speed of the rat and of the target are shown as the black and gray lines respectively (Adapted from manuscript Klement and Blahna, unpublished data).*

as the local minimum. If we had chosen a different definition of the beginning of navigation - the moment of the last acceleration before the end - then all the trajectories of this rat would look similar. Usually, smooth navigational trajectories are preceded by a sharp turn. Trajectories before this turn seem to be unrelated to the target (see the white trajectories in the 1st column in Fig.2.8.4). Similar behavior preceded the first acceleration in the tortuous trajectories in Rat 7. The trajectories between the first and the additional accelerations are clearly related to the target. The rat moves in the direction of the future contact with the target although along a tortuous path. Correspondingly the prediction error during this period fluctuates around zero. The second rat in Fig.2.8.4, Rat 5, approached the target along targetwise-curved trajectories only.

However, two of these trajectories can be divided into two parts (Fig. 2.8.4, 4th row). The rat swam initially far ahead of the target and then switched to the targetwise-curved trajectories. Rat 8 swam directly toward the place of contact. Its trajectories were straight especially during the first part of the navigation. During the second part the trajectories became slightly curved targetwise as the rat corrected its heading direction. The correction of the heading direction is visible in the time course of which increases during the second half of the navigation in all the trajectories of Rat 8. The oriented angle decreases almost linearly during navigation and the prediction error is negative but small.

We classified all the trajectories into the curved, straight and tortuous (Fig. 2.8.5). Seventeen (44%) were curved targetwise, 11 (28%) were straight and 11 (28%) were tortuous. The individual rats had the following numbers of the curved-straight-tortuous trajectories: 0-2-3, 1-2-2, 5-0-1, 6-0-0, 2-1-2, 3-0-3, 0-6-0. The classication was subjective. The differences among the three types were less clear compared to the trajectories in the slow sessions. We approximated the time courses of α, β and γ during the interval I (0.8 s after the beginning of navigation up to 0.2 s before the contact) by linear functions. Overall value of the angle α was changed during the navigation. In the start of navigation was α widely distributed but during the time concetrated around the value 30° (see Fig.2.8.6).

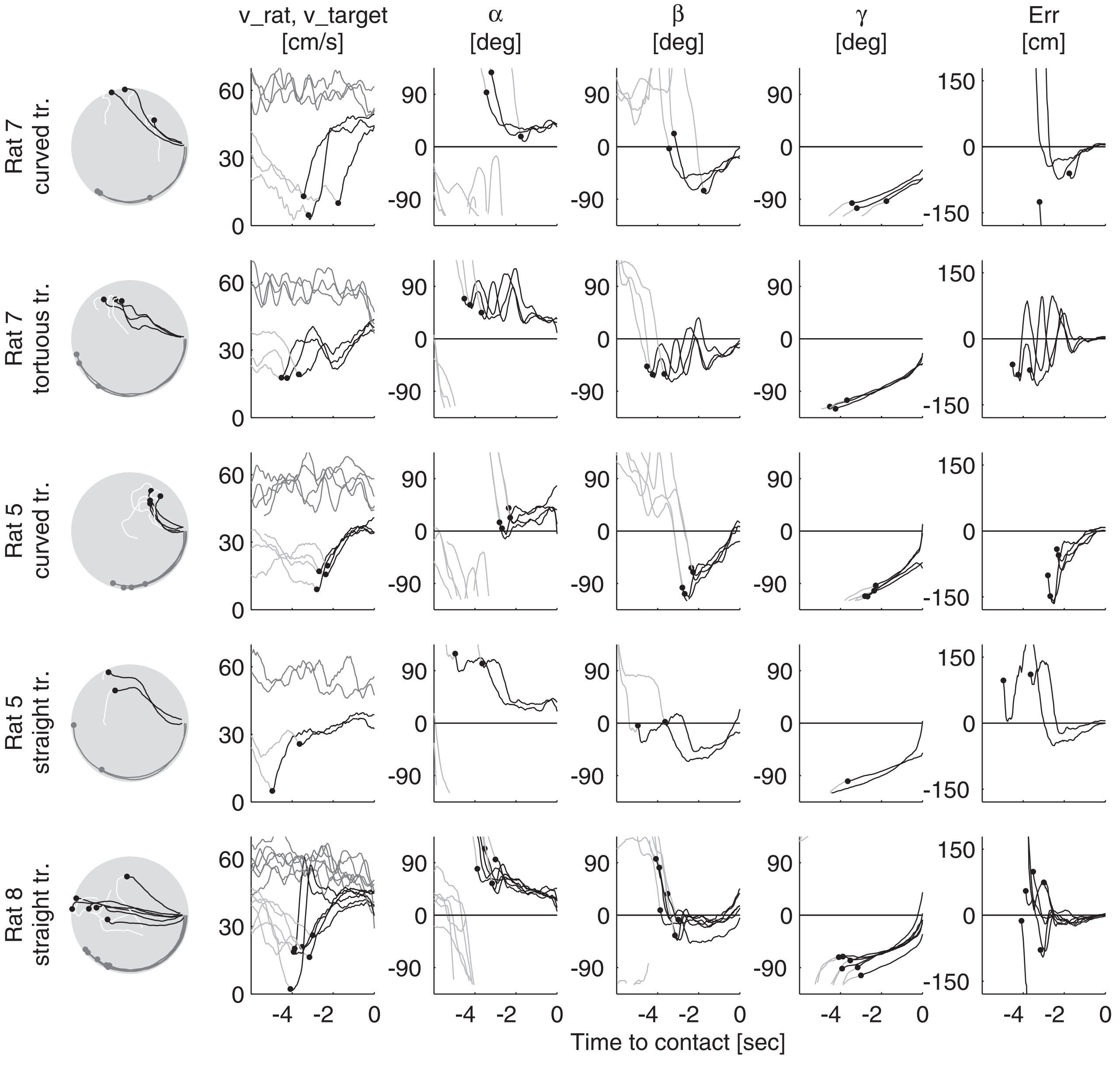


Figure 2.8.4: *Successful trials of three representative rats recorded in the fast sessions. The trajectories in the 1st column are transformed in such a way that the target moves counter-clockwise and the subject reaches it on East. The trajectories are divided according to their shape into curved, straight and tortuous. Beginnings of navigation are indicated by fill circles. Rat's trajectory (1st column) and time courses of the parameters v (speed),*α*,*β*,*γ *and Err (columns 2 to 6) during navigation is shown as the black lines. Rat's behavior before the navigational trials is depicted as the white lines in the 1st column and as the light gray lines in the other columns. Target trajectory (1st column) and its speed (2nd column) are shown as the gray lines (Adapted from Klement and Blahna, unpublished data).*

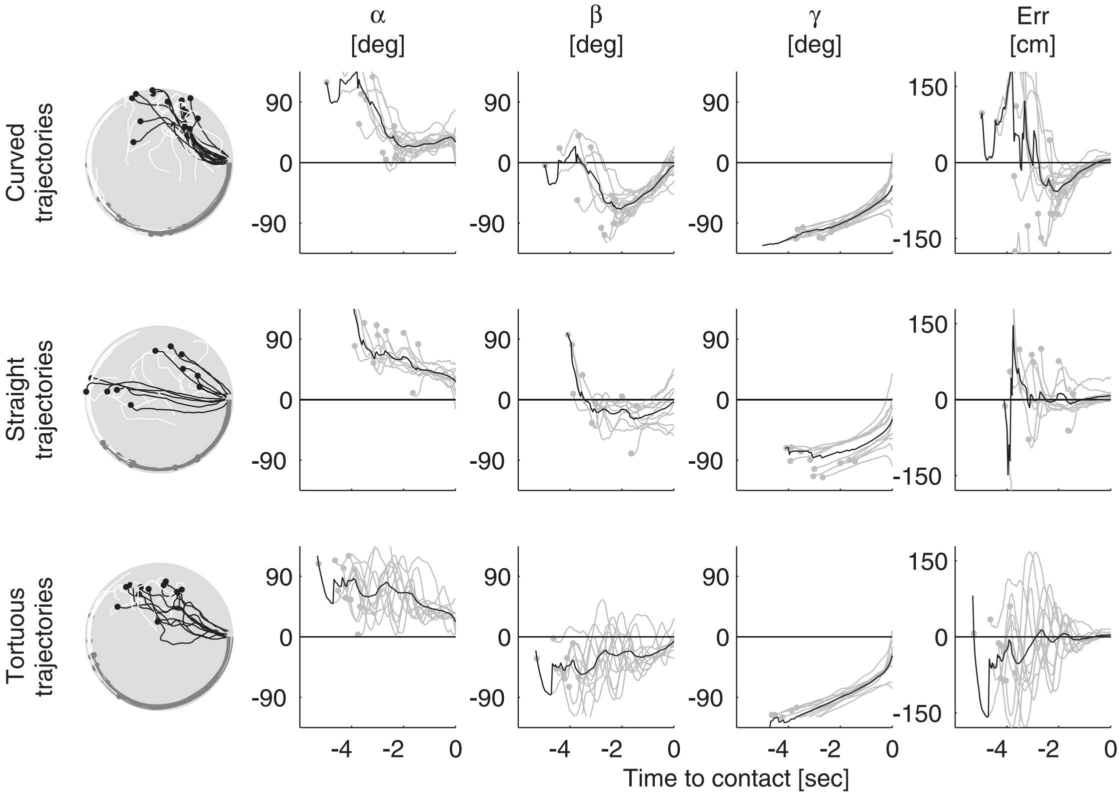


Figure 2.8.5: *All the successful trials recorded in the fast sessions. The trajectories in the 1st column are transformed in such a way that the target moves counter-clockwise and the subject reaches it on East. The trajectories are divided into three groups : curved, straight and tortuous. Beginnings of navigation are indicated by filled circles. Rats' trajectories before this moment are shown in white color in the 1st column. The columns 2 to 5 show the average time course of the corresponding parameter* α,β,γ *and Err as the black lines and the time courses of individual navigational trials are shown as the gray lines (Klement and Blahna, unpublished data).*

For the targetwise-curved trajectories the average value of α was 34.3±3.0°. It was greater than zero (one-sample t-test: $t_{16} = 11:34$; $P < 10^{-8}$). During this interval α increased with a rate of 2.9±4.2°/s however the increase was not significant (one-sample t-test: $t_{16} = 11.34$; $P = 0.49$). The anglesβ andγ increased during the interval with rates of 25.3±5.3/s and 22.4±1.8°/s, respectively. Both angles increased significantly (one-sample t-test: β: $t_{16}= 4.74$; $P < 10^{-3}$;γ : $t_{16} = 12.52$; $P < 10^{-8}$).

For the straight trajectories the average value offα was 46.8±2.3°. It was significantly greater than zero (one sample t-test: $t_{10} = 20.31$; $P < 10^{-8}$). Angle α was decreasing with a rate of -12.9±2.5°/s (one-sample t-test: $t_{10} = -5:09$; $P < 10^{-3}$). The angle β increased with a rate of 6.0±3.4°/s however the increase was not signicant (one-sample t-test: $t_{10} = 1.77$; $P = 0.11$). The angle γ increased with rates of 18.9±1.7°/s (one-sample t-test: $t_{10} = 11.22$; $P < 10^{-6}$).

For the tortuous trajectories the average value ofα was 58.8± 4.1°. It was significantly greater than zero (one sample t-test:$t_{10}= 14.35$; $P < 10^{-7}$).α was decreasing with a rate of -12.9±2.5°/s (one-sample t-test:$t_{10} = -3:60$; $P = 0:0048$). The angle increased with a rate of 6.8 ±4.2°/s however the increase was not significant (one- sample t-test: $t_{10} = 1.61$; $P = 0.14$). The angle γ increased with rates of 19.4 ±1:0°/s (one-sample t-test: $t_{10} = 19.73$; $P < 10^{-8}$).

2.8.2 Consecutive study

For an additional study will evaluate behavior of rats (n=5) trained during a consecutive 8 days to swim toward a moving target. 758 short navigational trials were obtained from all training sessions This study has focused on learning ability of animals to intercept the moving target. Each animal was trained for 18-21 short trials per day. Approximately 55 episodes were lost by means of unsuccesful navigation or technical problems. Rats had to start from steadily situated location marked by the metal rod. The movable robot was started up by the experimenter when animal touch the metal rod. Starting position of the robot was also predetermined according to the training protocol (described in Methods). Animals started from predetermined starting positions

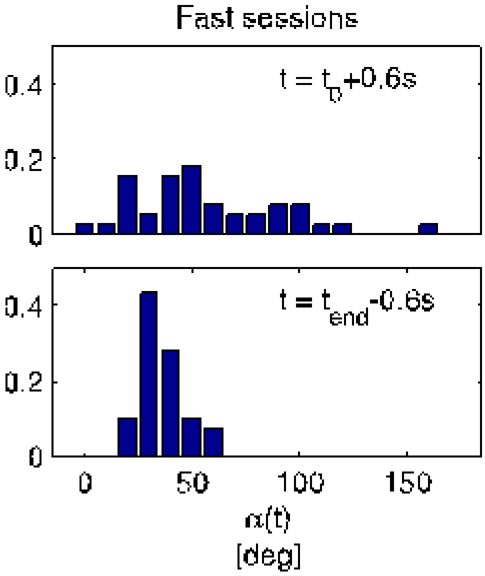


Figure 2.8.6: *Histogram showing that α was widely distributed at the beginning of navigation (upper graph) and concentrated around 30 degrees at the end of navigation (lower graph). t_o denotes the beginning of a trial, t_{end} the time of contact (Adapted from Klement and Blahna, 2006)*

in comparison to previous study. Average duration of one trial was in days 1-2: 2.82s ± 0.85 and in days 7-8: 3.09 s ± 0.96. Average velocity of moving target was for days 1-2: 25.1 cm/s ± 2.7, for days 7-8: 28.51±2.9. In spite of the slightly increase of the velocity, this velocity were still lower than maximum velocity of swimming rat. Average value of the rat speed of the swimming were in days 1-2: 40.2 cm/s ±4.9 and for days 7-8: 37.2 cm/s ±4.4. Average value of angle α was in general for days 1-2 4.95°± 14.2 and for days 7-8: 16.45 °±11.5. The value of α from the final part of navigational trial seems to be most important despite high fluctuations. Navigation in its final part became stable and most important for a succesful navigation. We compared angles α from the last 1600 ms of trials in the beginning and in the end of the training (see Figure2.8.7). The interval of 1600 ms was divided into four 400 ms intervals.The angle α was computed for each 400 ms interval. The angle α was higher in the end of the training (days 7-8) in comparision to the beginning of the training (days 1-2). Paired t-test was used for comparison of the angle α in the beginning and the end of training. We used Bonfferoni correction for multiple comparisons to keep the overall level the statistical test at 0.05. In the case the target moved along the circular trajectory (Fig. 2.8.7

A) and in the case the target moved along linear trajectory and the rat started from position B (Fig. 2.8.7 C) the difference was significant for all 400 ms intervals.Increase value of angle α could be caused by an increased speed of the target which slightly increased during training days 1-8. But this increase did not seems to be critical for the size of the angle α . Fig. 2.8.8 is showing that size of the angle α was changed with respect to the same values of speed of the target during training. Average values of the prediction error (Error) were in most of sessions across all days negative (see Fig.2.8.7, right panel). This indicates that animals obviously did not predict future position of contact with the moving target but rather processed angle α .

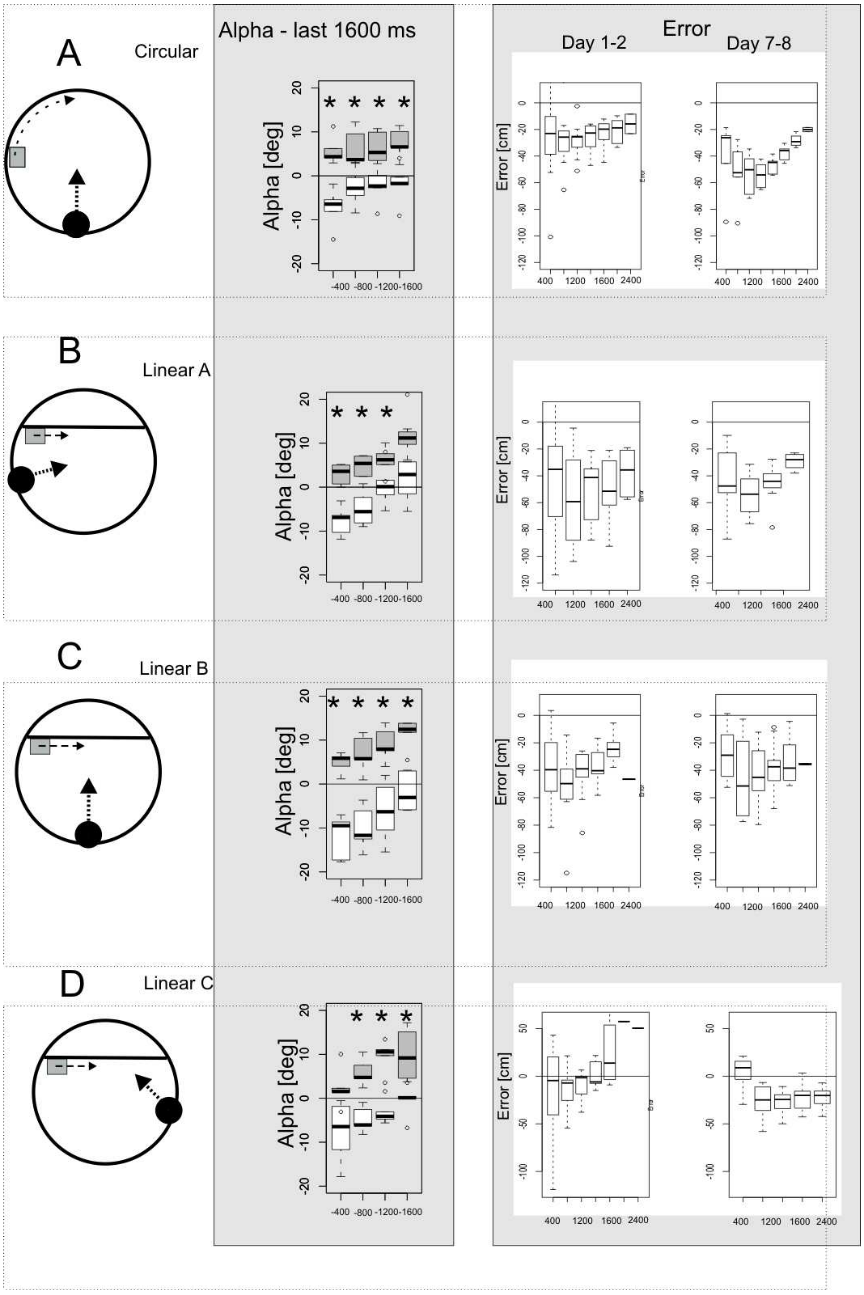


Figure 2.8.7: *Each row A-D represents configuration of starting position between rat and moving target. Left column: scheme of starting position between the rat(filled circle) and moving target(square). Middle column: boxplots of average values of angle* α *from 400 ms consecutive intervals. Presented data are from the last 1600 ms of navigation. White boxes indicated average values from day 1-2 of the training, grey boxes indicate average values from 7-8 day of training. It is obvious that final value of angle* α *has increased during training. This difference was significant in most cases. Asterisk indicate* $p < 0.05$ *for all values. Columns on the right presents values of prediction error from the inital phase of navigation until the 2400 ms. Each 400 ms represents average values of error In most cases in both initial and final part of training are values of error under zero line, what indicates that rats did not predict position of future time of contact.*

In the present study we have also analyzed if rats intercepting moving target react to the changes of the angle α. We tried to evaluate relation between the time course of the angle α and its derivative dα delayed by Δ, $\Delta = 0$ ms, 40 ms, 80 ms,...,600 ms. For choosing the optimal delay interval Δ_{min}, we compared Pearson correlation coefficients $r(\Delta)$ between the time course of angle α and its delayed derivative d$\alpha(\Delta)$,$\Delta = 0$ ms, 40 ms, 80 ms,..., 600 ms (see Fig.2.8.9, A and B). $\Delta_{\mathrm{min}}$was defined as arg$min(\{r(\Delta), \Delta \in \{0, 40, 80...600\}\})$. This Δ_{min}at which the correlation coefficient reached the minimum, we calculated for all the navigation trials from the beginning of the training and from the end of the training (see Fig. 2.8.9,C). Value of Δ_{min} could by termed like a “reaction time” for changes of the angle α . It was 200 ms for most of the navigation trials (see Fig. 2.8.9,C).

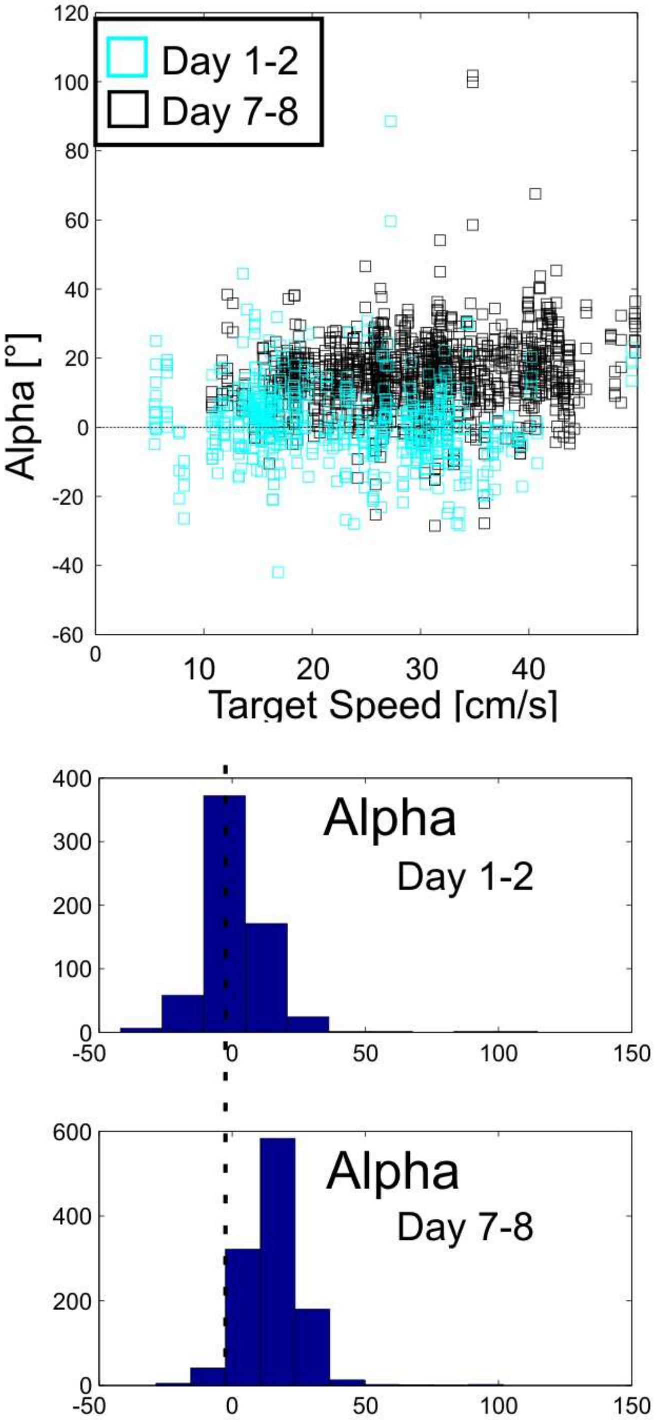


Figure 2.8.8: *Upper: Relationship between average values of the angle α from the last 1600ms of navigation. Presented values of angle α were already averaged inside a 400-ms bin. Each square represent average value of alpha inside one bin. Four last bins from each navigation trial are plotting with respect to the average speed of the target. Values from training days 1-2 are plotted in cyane color, values from training days 7-8 are plotted in the black color. Lower: Histogram of the angle α from the last 1600 ms of navigation for beginning (Day 1-2) and end (Day 7-8) of training. Presented are again average values of the angle α from each 400 ms bin. Histogram indicates that overall angle alpha has increased to positive values during training.*

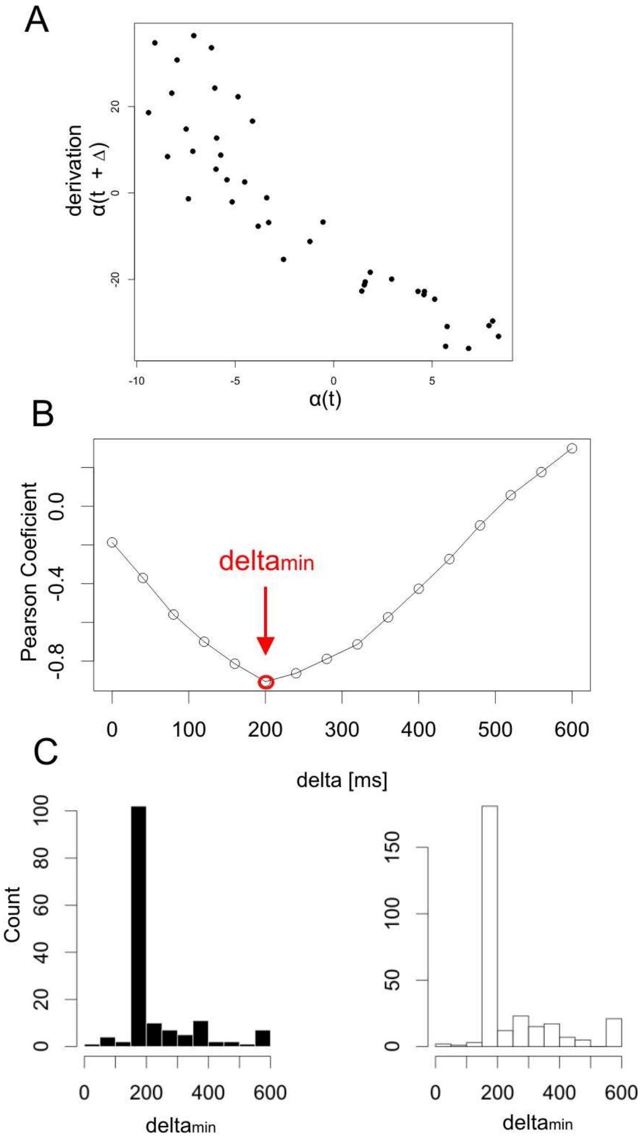


Figure 2.8.9: *A: Relation between the angle* α *(abscissa) and its derivative delayed by 200 ms (ordinate) during a typical navigation toward the moving target. B: Correlation coefficient between the angle alpha and its delayed derivative shown as a function of the delay (delta). The minimum is indicated by the red circle. In this example, the minimum was reached at delay 200 ms (=* $delta_{min}$*). C: Histograms of the delays at which the correlation coefficient reached the minimum calculated from all the navigations from begining of the training (left histogram) and from the end of the training (right panel).*

Part V

General discussion

2.9 Inertial stimuli in carousel arena

The behavioral task published by authors Blahna et. al (2011) was designed to test the role of inertial stimuli in the carousel arena (also referred to as active place avoidance) task.

Our results showed that inertial stimuli generated by arena rotation are important for learning the active place avoidance task. The rats trained on the rotating arena with the stable belt (the standard active place avoidance task – inertial stimuli were present) learned the task within six sessions. On the contrary six out of seven rats trained on the stable arena with the belt rotating around the arena (the modified active place avoidance task – the inertial stimuli were absent) did not learn the task. The two tasks were identical except the presence or absence of the inertial stimuli. It has been shown that inertial stimuli are important for spatial orientation (Etienne et al. 1980, Etienne et al., 1986, Glasauer et al. 1994, Matthews et al. 1989, Mittelstaedt 1980, Mittelstaedt et al. 1991, Potegal et al. 1985, Wallace et al. 2002, Wang et al. 1999). If an arena is suddenly rotated together with an animal, then the animal compensates for the rotation and navigates with respect to the stable experimental room instead of with respect to its new body orientation or to olfactory and tactile cues located on the arena (Etienne, 1986, Mittelstaedt and Mittestaedt, 1980).

The natural preference for using a stable reference frame during navigation is in agreement with our result. In both tasks, the rats could represent their position with respect to the belt where the to-be-avoided sector was defined or with respect to the arena. In the standard task, the belt reference frame was stable. The rats learned this task easily. On the contrary, in the modified task the belt reference frame was rotating. The rats, except one, did not learn this task.

We showed that, in order to learn the active place avoidance task, the to-be-avoided sector had to be defined with respect to a stable reference frame only during learning. The rats, which mastered the standard task, reached the same level of performance in the modified task. We suggest that in the beginning of the training the rats needed to perceive the extra-arena cues, which defined the location of the to-be-avoided sector, as stable. Once these cues became anchored into the representation of the environment together with the location of the to-be-avoided sector, the rats used these cues for navigation even when the cues were moving. Currently, we are testing this idea by training naive rats to avoid a sector on a stable arena. After the rats have learned the location of the to-be-avoided sector (it means after they have created the representation of the environment with visual landmarks and the location of the to-be-avoided sector incorporated in it), we trained them to solve the modified active place avoidance task. Preliminary results indicate that these rats solve the modified active place avoidance task.

It is possible that rats can learn the modified active place avoidance task after they have created representation of the environment with extra-arena cues incorporated in it but without the representation of the location of the to-be-avoided sector. We consider this idea as unlikely. All the rats presented in this paper were habituated to the arena in two 5 to 8 minutes sessions. The arena as well as the surrounding environment was stable during these habituation sessions. Thus the rat had time to create representation of the environment with the extra-arena cues anchored to it. Despite of it they did not learn the task except one rat. We do not know why one rat learned the modified task without the prior training in the standard task. Possibly, it is a matter of likelihood whether a subject will associate positions at which aversive stimuli were delivered with the moving extra-arena cues. Selection of the right subset of cues brings the subject to the solution of the task.

It has been shown that rats can navigate with respect to continually moving proximal cues and at the same time with respect to stable distal cues (Fenton et al. 1998). To our knowledge, our experiment showed for the first time that rats can navigate with respect to continually moving distal cues.

The standard active place avoidance task is hippocampal dependent (Cimadevilla 2000a). In the introduction part was described role of inertial stimuli, especially vestibular stimuli, with respect to important for function of the hippocampus. Deafferentation of vestibular input causes a 17 % decrease of hippocampal volume in humans, impaired performance in hippocampus dependent spatial tasks (Allen 2007, Matthews 1989, Stackman 2002a, Zheng 2007) and disturbed position-specific activity of hippocampal place cells (Russell 2003, Stackman 2002b).

Soliciting question is if instability between the relevant oriented cues and the inertial stimuli could have an impact on coding information about environment in the brain. Previously, Zinyuk et. al (2000) studied activity of place cells on a rotating arena. They described place cells with firing fields bound to the arena frame, bound to the extra-arena frame or to both frames simultaneously. The proportions of these place cells depended on the previous experience. Large majority of firing fields were bound to the arena in rats previously trained to chase for randomly scattered pellets. The proportion of firing fields bound to the extra-arena frame was higher in rats trained to orient with respect to the extra-arena frame (Fenton 2003, Zinyuk 2000). To our knowledge, there is no study addressing activity of place cells recorded on a stable arena while all extra-arena cues are continuously rotating around the arena. It is important to note for this type of environment, that animals can feel instability between visual and inertial sources of information. We can only suppose about neuronal activity of the rat's place cells network in the modified version of the task. The network of the place cells could behave in the similar manner like the neurons in the study of Sharp et al. (1995). The authors have studied the effect of fast and brief rotation of the arena floor or the arena wall on the activity of the place cells. When the arena floor rotated and the arena wall was stable, then most of place firing fields remained stable with respect to the arena wall, it means with respect to the stable reference frame. And vice versa, when the arena wall rotated and the arena floor was stable, then majority of the place fields remained stable with respect to the stable arena floor. Sometimes place cells firing fields shifted to the same direction as the direction of rotation of the unstable reference frame. This shift became more apparent as the subject repeatedly experienced the rotational manipulation. These results indicated that the activity of the place cells was preferentially bound to the stable reference frame when a brief rotational manipulation was introduced.

Vestibular information also drives a directional firing of the head direction cells (Taube 2007).

This system is functionally coupled together with place cells (Knierim 1995, Knierim 1998). It has been well documented that direction specificity of the head direction cells is controlled by visual landmarks together with information about inertial inputs (Taube 1990, Zugaro 2000, Goodridge 1998, Muller 1987, O'Keefe 1978, O'Keefe 1987). The strength of the cue control by head direction cells could depends on the cue stability (Knierim 1995). To our knowledge, there is no study addressing activity of head direction cells recorded on a continuously rotating arena, not to mention while all extra-arena cues are continuously rotating around the arena. We can hypothesize that sufficiently large number of place cells and head direction cells is bound to the extra-arena cues in the standard avoidance task (Group A, sessions 1-6, Fig. 2.5.1). In the modified task the majority of the place cells and head direction cells would be bound to the arena, mainly for the first phase of the training (Group B, sessions 1-6, Fig. 2.5.1). In case when the representation (place cells and head direction cells) of the environment become anchored, instability of the extra arena cues could not influence this representation (Group A, session 7 - 12, Fig. 2.5.1).

The inertial stimuli generated by arena rotation may have an additional role in the active place avoidance task to that of providing information which reference frame is stable and which is moving. Perception of accelerations and decelerations by the vestibular system, proprioceptors and skin mechanoceptors conveys information to a subject that its position is changing, that new information may be coming and new responses required (Smith 2010). This information is processed automatically without attentional demands (Yardley 2002). Thus a moving rat may perform better in spatial tasks because it is ready to process information and to generate responses (Smith 2010). This idea becomes interesting after realizing that most of the time rats do not actively move during the active place avoidance task (the rats in the present study were sitting 60 % of the time of the sessions). As we discuss below the rats were sitting at the critical moments when they should generate escape reactions.

Detailed observation of trained rats during the standard active place avoidance task showed that they alternate two behaviors - sitting and running. When a rat is sitting, arena rotation transports it towards the to-be-avoided sector. Before the rat enters the to-be-avoided sector it initiates an escape reaction. The escape reaction is most frequently a run against the arena rotation. The rat stops running before it enters the to-be-avoided sector from the other side. The alternation of sitting and running is characteristics for all the successful solvers of the place avoidance task we have analyzed so far (Klement et al. unpublished results).

Due to the arena rotation, the rats perceived inertial stimulation during the sitting period in the standard active place avoidance task but not in the modified active place avoidance task. It is an open question whether the lack of inertial stimulation during the sitting period in the modified task decreased the ability of the rats to learn the task. This question can be answered by motivating rats to actively walk in the modified active place avoidance task, e.g. by searching for food pellets. The present experiment shows that rats are not able to use all reference frames in the same way during acquisition of the spatial task, e.g. rats will rarely use a reference frame defined by a moving object for determine positions in their environment. In a pilot study we failed to condition rats to avoid a sector on an arena defined with respect to a single salient object rotating around the arena (see Appendix Fig.2.12.1). Ho et al. (2008) showed that hippocampal neurons do not form a representation of the environment with respect to a moving object but they encode various movement parameters of the object such as speed, direction of movement as well as the distance between the subject and the object. In presented enemy avoidance task, rats can orient in the reference frame defined by the moving object. Results from pilot task indicate that only a small number of rats would do it unless this object would be stable during learning. Moreover, rats trained at first in the modified version with a lot of cues outside the carousel arena task, were not able to utilize position of the sector.

We conclude that the inertial stimuli generated by arena rotation are important for acquisition of the active place avoidance task but not for performance once the task has been mastered. We suggest that rats must perceive the distal extra-arena cues as stable in order to reliably associate position of the to-be-avoided sector with these cues.

Vestibular component perceiving in carousel arena Solicit important question is about threshold of perception of vestibular inputs. As described above in section of method, rotation of our arena was 1 rpm, what is approximately 6° per second. Animals in standard version of the task were running or sitting on rotating arena. There exist only small number studies discussing threshold of perceiving vestibular stimuli by rodents which are moving passively (Mittelstaedt and Mittelstaedt 1980, Jeffery 1998). The authors only excluded possibility that animals should perceive passive transport on the arena. However, there are known some values of perceiving of passive displacement from studies in monkeys (Sadeghi et al. 2007a). When the head of the monkey was displaced by the regular movement, threshold for perceiving was approximately 4° per seconds, when the movement was irregular, the threshold was increased to 8°per seconds. From my subjective observation, our experimental arena rotated regularly but sometimes with small irregular oscillations. Moreover, our animals run thru the all surface of the arena, and centrifugal force differ with increase distance of the center. We supposed, that animals could perceive vestibular inputs, however arena also generate inertial stimuli which are perceived by proprioceptors and tactile receptors.

Sensory mismatch and motion sickness Exposure of the animals to the modified version of the task apparently leads to a conflict between the self-motion cues and distal navigation landmarks. Both groups of animals were previously habituated on the stable arena which during training started rotate. Animals from control group had perceived instrumentality of inertial stimuli from rotating arena together with an accordant optical flow. Animals from the second group were for the first time exposed toward the whole world rotated around the stable arena. It is possible that rats perceived motion sickness rising from the sensory mismatch between visual and vestibular or proprioceptive inputs. This phenomenon has been already described in humans (Stern et. al. 1989) and as well as rodents (Uno et al. 2000, Zou 2009). We are not able to exclude the possibility that rats in the modified task perceived the motion sickness. The activity of animals did not differ in both versions of the task. Hypothetical motion sickness does not influenced performance of the control animals.

Competition and cooperation between visual and inertial inputs An alternative explanation could be also given to clarify discrepancy of performance between animals initially trained in the classical version and the modified version of the task. As we saw above, processing of spatial information is based mainly on the system for positions and on the system for estimating the directions. First system is primary represent by cells from the hippocampus and the entorhinal cortex, second one is based on the head direction system distributed in many areas. As we mentioned in the introduction part, head direction system is interconnected with complex of vestibular nuclei, and very probably mediate interaction with hippocampal formation. Two types of neurons from vestibular nucleus complex has been studied in monkeys. These neurons differed by their responding to movement stimuli, e.g. vestibular and visual. First type of neurons were sensitive to vestibular or optokinetic stimuli. Second types of neurons were sensitive only when both types of stimuli were presented. We can only speculate how neurons in vestibular nucleus could behave in rats performing the classical or modified version of the AAPA. Also signal from the vestibular nuclei complex could be the most critical for organizing relations between optokinetic and vestibular information. Discordance between perceiving visual and vestibular information in animals which were at first exposed to the modified task can induced disorganization between neurons in complex of vestibular nuclei and consequently in system of head direction cells and also in the hippocampal formation (See also scheme with interconnection between the vestibular nuclei complex, head direction cells and hippocampus in Figures: 1.2.5, 2.0.8).

2.10 Role of the posterior parietal cortex

Study by Svoboda et al. (2008) evaluated the role of the posterior parietal cortex in the carousel arena task. The authors hypothesized that animals without functional PPC will show a deterioration of the processing of spatial information from the arena reference frame. The arena frame consisted of visual and olfactory cues as well as the self-motion cues derived from locomotion. Previous studies pointed to involvement of the posterior parietal cortex in processing information mainly about proximal cues in the environment (Save and Poucet, 2000, Rogers and Kesner, 2006). Electrophysiological studies also suggested involvement of cortical neurons in processing of spatial information about cues oriented relativelly to the immobile subject (Nakamura 1999). However, the same study also showed that some of these neurons were also bound with respect to allothetic cues on the arena. A recent study by Save et al. (2005) showed that PPC is functionally coupled with hippocampal place cells. When distal cues were manipulated, place cell activity in animals with lesion of the PPC has not been affected. This was most remarkable when distal landmarks wer shifted. In normal animals, firing activity of place cells was abolished, but it was intact in animals with lesion of the PPC. These results suggested inability of the lesioned animals to use the proximal cues for "tuning" of the place cell activity (Save et al. 2005). Our study; however, revealed no significant participation of the PPC for efficient performance in both versions of carousel task (arena-frame or room-frame defined sector). It should be noted that the carousel task does not require a high degree of spatial accuracy in processing of spatial information compared to e.g. Morris water maze. Instead, this task requires high degree of stimuli segregation and oriented attention. Some studies on primates demonstrated a role of the posterior parietal cortex in working memory and attention (see Bucci, 2009).

It might be speculated that this version of carousel test is not sensitive enough for detection of impairment induced by PPC lesion. Moreover, our results suggest that parietal cortex is not important for segregation of spatial information. These result also well support our recent and unpublished observations in double place avoidance task. This is the version with the highest degree of the segregation demands. In this task, animals animals had to simultaneously avoid two sectors defined by the arena and room reference frames (see also in Figures 2.0.4, 2.0.5 C). It would be also interesting to evaluate the role of the PPC in the behavioral protocol with the modified version of the carousel task without inertial component, which was described above. We presuppose that removing of the inertial component in the carousel arena could affect the performance of the animals with PPClesion . As shown in figure 1.2.5, the parietal cortex is interconnected with system of head direction cells (and this system in turn with with vestibular system) as well as with system of hippocampal place cells. Animals without PPC can be less sensitive to subtle changes when inertial stimuli are suddenly lost but when optic flow and landmark information remains constant. This hypothesis would be supported by the fact that PPC can integrate self-motion and inertial cues with visual and olfactory information.

2.11 Summary and outlooks for future research

The study of Blahna et al. (2011) has shown that inertial stimuli play necessary role in learning process in a dynamic environment with dissociated reference frames. Once the ability to learn the task was mastered, however, animals could perform the task without inertial stimuli. In future research, we can test the roleof the optic flow in this configuration. We can also evaluate brain systems interconnected with vestibular system, head direction system, place cell systems and the posterior parietal cortex.

2.12 Rat´s interaction with moving target

2.12.1 Enemy avoidance task

The second type of the dynamic world differs from the previous in several aspects. Dynamic world on the carousel arena arises from dissociation of two independent reference frames. During rotation of the carousal arena, animals perceive many cues as unstable. Dynamic world, which represents one moving object, usually takes place only inside one reference frame. We developed two new behavioral tests for studying behavior of rats interacting with a moving object. In the first task rats avoided moving object on the stable arena and in the second task they navigated towards a target moving along the periphery of the water maze.

Avoidance task – a behavioral component In the first behavioral paradigm – Enemy Avoidance Task (Telensky et al., submitted) was "subject rat" avoided another "conspecific". In the subsequent study (Telensky et al., submitted) "subject rat" avoided programmable moving robot. Rats were trained to continuously avoid a moving object (a conspecific or robot) while continuously foraging pellets on the experimental arena. We observed general reaction when negative reinforcement (mild electric shock) was introduced. Rats rapidly adopted hypolocomotion and elevated thigmotaxis (preference of walls) in both "conspecific" (Fig.2.7.2) and "robot"(Fig.2.7.4) versions of the task. Thigmotaxis behavior is extremely adaptive in wildlife especially in situations when rodents are confronted with occurrence of a predator (Edut and Eilam, 2004). This reaction is effective, because thigmotaxis behavior may decrease the probability of the encounter between the animal and the predator. Thigmotaxis is not seen only in the wildlife, but also abundantly observed in experimental environments. Animals confronted with aversive task as the Morris water maze very often swim along the walls of the maze (Morris 1981). On the other hand, anxiety resulting from initial exposure to swimming (which may be first such episode in the laboratory animal´s life) may also contribute to the expression of this behavioral pattern. When rats start to comprehend rules of the task, thigmotaxis disappeared (see also Morris 1981, Whishaw 2005). Decrease of locomotion after administration of the shock in animals foraging pellets in the open-field arena was described previously (see for example Stuchlik and Bures 2002). Both increased thigmotaxis and decreased locomotion contributed decrease of the probability of contact between rats and the moving object. However, these two immediate reactions of rats were not sufficient for efficient performance of the task. Rats, which had avoided a conspecific, significantly decreased their overall locomotor activity. Nonetheless, together with increasing experience animals improved their ability to avoid another rat. It was shown by the average increase of the locomotion between two entrances into the denied region defined by the conspecific (See Fig.2.6.1). Rats trained to avoid the moving robot (M group) behaved in the similar manner. Their thigmotaxis has increased and locomotion has decreased in the very beginning of the training (see Fig.2.7.4). Control rats, which avoided stable robot (S group), did not show such extent of thoimotaxis and their locomotion was significantly higher than in animals from the M group (see Fig.2.7.4). To exclude the possibility that the S group animals could associate the shock area with some cues inside or outside arena was ruled out changing the robot position to in the middle of each session. This difference between the M and S group pointed for the stronger adaptive reaction of rats from M group to avoid moving robot.

In spite of immediate, adaptive and probably innate reactions, the process of avoidance learning developed across training sessions. This pointed to the learning component of this behavioral task. In comparison with standard avoidance task on the carousel arena (see Fig.2.5.1) rats trained to avoid a conspecific required longer learning (See fig.2.6.1). This fact was probably caused by innate social interactions that may have occurred between the "subject rat" and a conspecific which frequently caused nearer close contact (see Fig.2.7.2). Results also pointed to more active behavior of a conspecific rat than subject rat before footshock administration. This was the main reason why we decided to replace a conspecific with an artificial object - the moving robot. Learning to avoid moving robot was faster than acquisition of avoidance of a conspecific (see Fig. 2.7.3) and therefore we have used this protocol for a consecutive lesion study.

Avoidance task – role of the hippocampus

We also tested the role of the hippocampus in the robot avoidance task. When rat has reached the learning asymptote, we re-tested them after the temporal inactivation of the dorsal portion of the hippocampus by TTX. This study showed that rat hippocampus plays an important role for avoidance of moving target. Interestingly temporal inactivation did not influence avoidance of the stable robot. This is in disagreement with Cognitive Map theory (O´Keefe and Nadel 1978, Morris et al. 1982) and also with Declarative Memory theory (Scoville and Milner 1957). Our results pointed to engagement of hippocampus in flexible dynamic world. In this world position of moving object continuously changes its location and obviously hippocampus supports rapid representation of actual places and also updates actual locations of a moving object. We can also exclude the idea that TTX inactivation of the hippocampus impaired sensitivity or escape reaction to the footshock. Animals which were trained to avoid stable robot were not after the temporal inactivation of the dorsal hippocampus abolished in avoidance behavior.

Histological control (see Fig.2.7.5) showed that infusion needles were situated in the correct places and orientation ink infusion test did not suggest possible spreading of the TTX to the neighboring areas. Hypothetical influence of the TTX of the locomotion was also excluded because the locomotion of the S group of rats was not decreased. The present data also excluded the idea that hippocampus is not important for estimating distances between the rat and the stable objects. There exist only a few studies discussing the role of the hippocampus for estimation distances between cues in space (Long and Kesner 1996, 1997). Deficit of avoidance ability in the M group of rats indicate rather an inability to process complicated changes of position of robot than distances. The fact that avoidance of the stable visible cue is not hippocampus dependent is in accordance with the Cognitive Map Theory (O´Keefe and Nadel 1978, Morris et al. 1982). This theory presupposes that navigation toward the visible cue is not hippocampus dependent. Novel contribution from our study is that temporal inactivation of the dorsal portion of the hippocampus abolished representation of moving but still visible object. In general, hippocampus is brain structure with high computational potential and we believe that its role is not clearly for representation of locations in a stable space. This structure could be also responsible for flexible updating of actual changed positions of unstable visible cue.

2.12.2 Navigation towards the moving target

The manuscript written by Klement and Blahna showed basic findings about the interception abilities of rats. Present study was already submitted to the Journal of Experimental Biology and recently the authors have revised the manuscript.

In this task rats were trained to catch a moving target. The target moved with a constant speed along the wall of a circular water pool. If an animal waited at the wall or swam along the wall toward the target then the target was lifted up to become unavailable until it passed the animal. Thus the animals were forced to navigate across the inner part of the pool. The target moved either slower (slow sessions) or faster (fast sessions) than the maximum swimming speed of the rats.

A rat can reach a moving target by controlling speed and direction of its movement. Therefore we analyzed momentary speed and heading direction of the rats during ses sions. In the slow sessions the rats initiated navigation by accelerating their swimming speed. The navigation lasted around 3.3 s. The trajectories were either curved in the direction of target movement (72%) or they were straight (28%).

If the rats swam along the curved trajectory then they headed toward the target (average value of α during navigation was zero). This relative heading direction slowly increased during navigation with the rate 4/s. The increase could be possibly caused by navigation directed toward the front edge of the target. We propose that the curved trajectories can be explained by the pursuit strategy in which a subject moves toward the visible target.

The straight trajectories are characterized by approximately constant time courses of α, β and γ. They can be explained by different strategies - prediction (β constant), CTHA (constant target heading angle: α is constant) or CATD (constant absolute target direction: γ is constant). All these strategies result in the same shape of target approaching trajectory if the target moves with a constant speed along a straight line (Fig. 2.4.1.A). In the present task the target trajectory was circular however it was short and thus only little deviated from a straight line (e.g. Fig. 2.8.1., 1st column). It is not necessary to keep an absolute value of α or γ during navigation in order to reach the target. A subject might keep some value and if it changes for any reasons then the subject might fix the new value. In this case the subject nulls changes in the controlling variable. Figure

2.8.2 indicates that in both types of trajectories the rats null the changes of angle α. Thus it is possible that α was important for guiding the rats in both types of the trajectories and only the absolute value around which the changes were nulled made the difference between the curved and the straight trajectories. This view favors the CTHA strategy over the others. However, Ghose et al. (2006) showed that bats (*Eptesicus fuscus*) null changes in γ when they are hunting an erratically moving insect. Due to this strategy a bat does not have to change orientation of its head with respect to the environment while echolocating its prey. Fajen and Warren (2007) showed that target-approaching behavior of humans to a linearly moving target is best explained by the strategy in which subjects null changes in γ. We cannot rule out the CATD strategy, nevertheless, in the context of our experiment might be α more important than γ. The rats are in a circular environment with no orientation cues on the wall of the maze. The most salient and important cue is the experimenter walking around the maze. The other possible strategy - predictive strategy has some limitations. As it has been mentioned, the animal must precisely estimate variables upon which the prediction is made and the target should not change its movement. We tried to make the target movement predictable, nevertheless, the strategies exploiting perceptuomotor feedback are more robust and thus preferable in the case the navigation lasts longer than hundreds of milliseconds (Tresilian, 2005). The possible way how to distinguish among these strategies in the present experiment is to increase target speed in order to make its trajectory more circular however the increase speed should remain lower than the maximum swimming speed of rats. The rats were also trained to navigate toward the fast-moving target. In this case it was not possible to reach the target by swimming toward it. Thus the rats learned to swim ahead of target movement in the fast sessions. It is not clear whether this training facilitated the appearance of the straight trajectories in the slow sessions. In the fast sessions the rats usually needed several attempts to catch the target. We analyzed the successful attempts only. The beginning of a successful navigation was taken as the moment of the earliest acceleration followed by target-directed movement during which the subject kept between 15° and 150° until the end. The successful navigations lasted around 3.3 s. We classied the navigational trajectories according to their shapes as curved in the direction of target movement (44%), straight (28%) and tortuous (28%). At the end most of the trajectories were smooth and at least slightly curved in the direction of target movement. The difference among the three types was in the first half of the trajectories.

Before the final navigation, the rats swam to a place where they started the navigation. The path toward the place seemed to be unrelated to the target (Figs 2.8.4, 2.8.5). Nevertheless it is possible that the rats recognized the place as feasible for the navigation. The curved trajectories were similar to the curved trajectories recorded in the slow sessions. The rats continually updated their heading direction and the target-heading angle rose slowly during the navigation (2.8/s). Unlike in the slow sessions the average value of α during navigation was tens of degrees above zero. The continuous and smooth update of heading direction together with monotone speed increase points to a close-loop algorithm which is computational simple. It is possible that was the controlling variable in this algorithm.

The tortuous trajectories were tortuous only during the first half. During the second half they became smooth. The moment of the switch from the tortuous path to the smooth one was visible in the speed profile as an additional acceleration. During the tortuous part the rats updated their heading direction in such a way that the prediction error oscillated around zero. The rats fluctuated around a straight line toward the place of contact. The speed profile contained temporary decelerations. Such behavior points to a perceptuomotor close-loop algorithm as it was in the curved trajectories however in this case the rats likely did not produce a simple response to an easily perceived controlling variable like α. It is possible that the rats repeatedly estimated (predicted) where they can meet the target and corrected their behavior accordingly. The time course of α can be approximated by a decreasing linear function around which it fluctuated. Moreover in the consecutive study we described the time delay Δ_{min}= 200 ms, which seems to be critical for processing changes of angle α and correcting heading to a new value of this variable.

The linear decrease of $\alpha$was also present in the straight trajectories. In this case the trajectories were smooth and the speed profile was increasing. Such behavior does not indicate any time-consuming calculations during the navigation. It is possible that the rats decreased α with constant speed during navigation. A similar view has been used to explain the target-approaching behavior in humans catching a flying ball in so called OAC strategy in which the subjects guide their movement to change perceived angles with increasing, decreasing or constant rates (McLeod et al., 2006). Despite the theory fits experimental data, it is not clear whether humans or rats in our case can perceive the angular changes with sufficient precision (McBeath et al. 1995). Other possible explanation of our data is prediction taking place before the onset of navigation or some kind of stereotyped behavior in which unsuccessful navigation brings the subject close to the target and from this point the subject starts its movement across the pool to catch the target on the other side of the pool. As the subject gets close to the target it starts to change its heading direction and either catches the target or misses it (Fig.2.8.5). This behavior ensures that the rat always starts navigation from similar positions with respect to the target. After missing the target the subject can adjust its behavior by speed increase or by swimming more ahead of the target movement.

Originally, the rats were trained to start their navigation from a stick located in the center of the pool. If they missed the target then they had to return to the stick to make the target available again. This procedure helped the rats to navigate across the inner part of the pool. Rarely they waited at the wall or swam toward the target along the wall. Later we trained another group of rats without the stick in the early phase of training. These rats were confused when the target was suddenly lifted up in front of a waiting subject. Their navigational trajectories were very short in the fast sessions (data not shown).

In the consecutive study we trained a small group of rats (n=5) navigate toward a moving target with modified experimental protocol. The protocol was built up to enable tested: Potential importance of mutual positions between the rat and the moving target and difference in navigation toward the target moving along both circular or linear trajectory (Fig 2.4.2). Aim of this study was also to test learning process of interception.

Starting positions The reasons why we decided to design this experiment with mutual tightly fixed starting positions between the rat and the target (Circular, Linear A-C) stem from results of pilot experiment. As mentioned above, the rats always started their successful (but also most of the unsuccessful navigation trials - data were not presented) from similar positions located with respect to the moving target. Notable is that rats have chosen these places willfully. In our previous analysis we also try to model previously above described navigation strategies of keeping constant change of angle α in the enclosed circular environment. Artificial trajectories and mainly their starting positions produced by this model were distributed only for restricted areas in the circular area maze. When we fitted our real data to this model, starting positions of navigation trials fitted well into the model (Blahna and Klement 2008). In the consecutive study we wanted to test, if different configuration of start places could affect interception behavior. If the starting position plays some important role for navigation, it could be expected potential differences of navigation trials for different configurations. These differences could be characterized for example by different values of angle α or different course of prediction error. Preliminary results did not demonstrate any differences in trials with different configurations of starting positions. Angle α has increased in all versions of test and negative values of the prediction error (Err) excluded prediction strategy in some from the configuration. Of course we observed several trajectories which had a straight course what could have an effect for predictive strategy (see Fig. 2.12.2) but in general, most of the trajectories seems to be related to process of angle alpha.

Curved vs Straight trajectories We decided to test the rats in both curved and straight trajectories of the target. The reason why we decided to test the animals so was to obtain some resolution about navigation strategies. We hoped that we found the resolution if the rats use more open loop (predictive) or close loop (keeping constant value or constant change of angle α) strategy. We expected more occurrence of the predictive strategy for the straight (and more predictable) trajectory of the target. Generally, most of their trajectories of rat navigation were rather curved than straight and course of parameter of prediction of error was negative and continuously increased (see Fig. 2.8.7 right column). All trajectories were similar in course of the angle α (Fig. 2.8.7left column and2.8.8 B). Results from this pilot experiment pointed to general usage of close strategy of regulating of the angle α for both shapes of trajectories of the target.

Learning of the interception We also wanted to explore if rats change their behavior during experience with the task. From above described experiments (e.g. in enemy avoidance task, or experiments where rats interact with moving environment, for review see Klement et al. 2008, attached in the thesis) is obvious that rats are able to learn various dynamic tasks. In the pilot experiment we analyzed behavior of the overtrained animals. In a consecutive study we studied behavior of naive animals which were trained in a consecutive 8 days. In this study training process was more controlled. We found that animals with increased experience more anticipated the goal, which was most obvious from the value of the angle α (Fig.2.8.7). This increase of anticipation does not mean prediction. The parameter of prediction error does not change during experience with interception and remained negative for whole training session (Fig.2.8.7).

We also analyzed specific time delay (called Δ_{min}) critical for the reaction of the rats to the changes of angle α (Fig 2.332.8.9). This time delay was surprisingly the same for most of the navigation trials. However this time delay did not change during experience of animals with interception of moving target.

2.12.3 Summary and future outlooks

We demonstrated that rats are able to interact with moving object. This ability developed during the time in both the avoidance and approach behavior paradigm. We also presented that hippocampus is important for avoidance of moving object.

Presented interception task is suitable for studying navigation of rats toward a moving target. To our knowledge this is the first behavioral task developed for this purpose in rats. The rats are commonly used to study neural mechanisms underlying various types of cognitive behavior. The task can also be used for studying neural circuits responsible for this behavior. It is not clear whether the hippocampus is necessary for any observed type of interception navigation. Previous described enemy avoidance task showed that dorsal hippocampus play an important role for representation of locations of moving robot. Above-mentioned enemy avoidance behavior does not require a precise spatio-temporal interaction between the rat and moving object. Instead of it, rats avoided the robot are motivated continuously search the moving object and navigate towards the location of the arena, where moving object will not appear. We can only speculate if rats for both types of behavior - avoidance of the object or navigation toward the moving goal using the same algorithms. Several authors assume that people in locomotion use the same algorithms of navigation when approach or avoid object (for overview see Warren 1998). I suppose that rat can utilize the same algorithm of process of angle alpha, as were described in navigation toward the moving target, during the escape phase when the moving object is approaching. If the hippocampus plays some fundamental role in the navigation toward the moving target is still an open question. Already mentioned work of the authors Ho et al. (2008) did not found any direct neural correlate for representing navigation toward the moving target in this structure. The authors used very simple pursuit behavioral model of navigation. This behavior did not require any computation engagement. The present results suggest that hippocampus is certainly involved in process of actual updating of the location of the moving object. Process of angle alpha and reaction of the head lasted very short time period 200 ms, what pointed rather to an engagement of a lower brain structures than a cortex or hippocampus, but this is still unanswered question requiring future study.

In future we want to evaluate engagement of other brain structures in the avoidance model (e.g. parietal cortex, striatum, and cerebellum). It would be also interesting to evaluate escape behavior of rats in avoidance model in more detail. We can also develop presented interception task. We would like to study engagement of hippocampus in this task. On the other hand, inspired by work of Schuster et al. (2008), we want to study fast decision making processes in navigation. Recently, we also finished analysis of rat navigation toward the moving target with an obstacle. Preliminary results from this study pointed to rat ability to continue in the correct navigation toward the goal, although this moving goal disappeared for the while. All these pilot data should be important for the future studies focused on the dynamic processes in the brain, which reflect dynamic world around as.

Part VI

Main findings of the dissertation

1. We have revealed the crucial role of the inertial stimuli for spatial avoidance in the dynamic world on the carousel arena.

Presence of inertial stimuli is important for spatial learning. We showed that inertial stimuli are important for initial phase of avoidance acquisition. Once memory had established, perception of inertial stimuli became unimportant.

2. We have developed two behavioral tests involving dynamic world in which rats interact with the moving object.

We have designed two behavioral tasks. First, enemy avoidance task enables automatic study of rats in dynamical environment with moving object. The task has shown that rats immediately react to moving object by thigmotaxis, decreased locomotion and avoidance. With increased experience animal have eventually learnt to avoid the moving object. Second task tested rat's ability to navigate toward the moving target in a modified water maze. This task has allowed us to study mutual interactions between the rat and the target into great detail.

3. We have shown no involvement of the posterior parietal cortex in spatial avoidance of an unmarked place defined by local or remote orienting cues on the carousel arena.

Posterior parietal cortex is not important for process of active place avoidance task based of either distal or proximal cues in carousel task.

4. We have revealed critical role of hippocampus in the avoidance of a moving object.

Temporal inactivation of the hippocampus affected ability of rats to avoid the moving object (mobile robot). Animals with temporal inactivation of the hippocampus which avoided stable object were not affected. These results point to the critical role of the hippocampus in continuous updating of information about position of a moving object in a dynamic task but also show that hippocampus is not necessary for distance estimation (which is required for stable robot avoidance).

5. We have suggested behavioral strategy that rats can utilize during navigation toward the moving target.

An important variable for processing of navigation towards a moving target is the angle between the direction of movement and hypothetical line connecting rat's head and moving target actual position (alpha angle). This angle increased during training. Rats reacted to changes of this angle with time delay of 200 ms. These results suggest usage of a so-called closed loop strategy by rats regulating alpha angle for prediction of a position of a moving target.

Part VII

Appendix

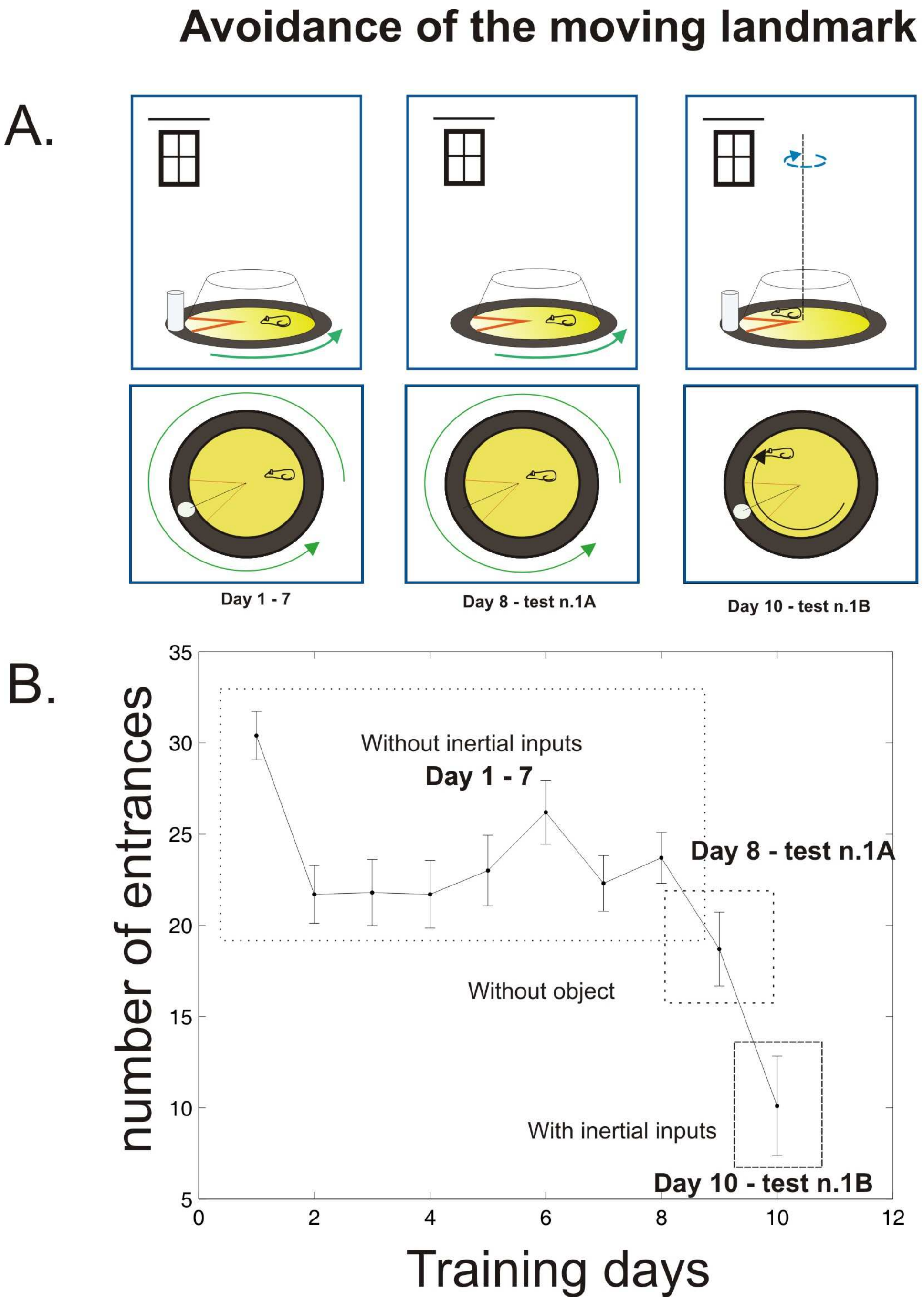


Figure 2.12.1: *Pilot study of the rat´s avoidance of a moving salient landmark. A: Scheme of the experiment. B: Days 1-7; the rats were not able to avoid a salient landmark moving around the stable arena. Their performance did not change, when the salient landmark was removed in day 8. The performance improved when inner arena started to rotate and salient landmark remained stable in day 10. Adapted from Blahna et al. (2007).*

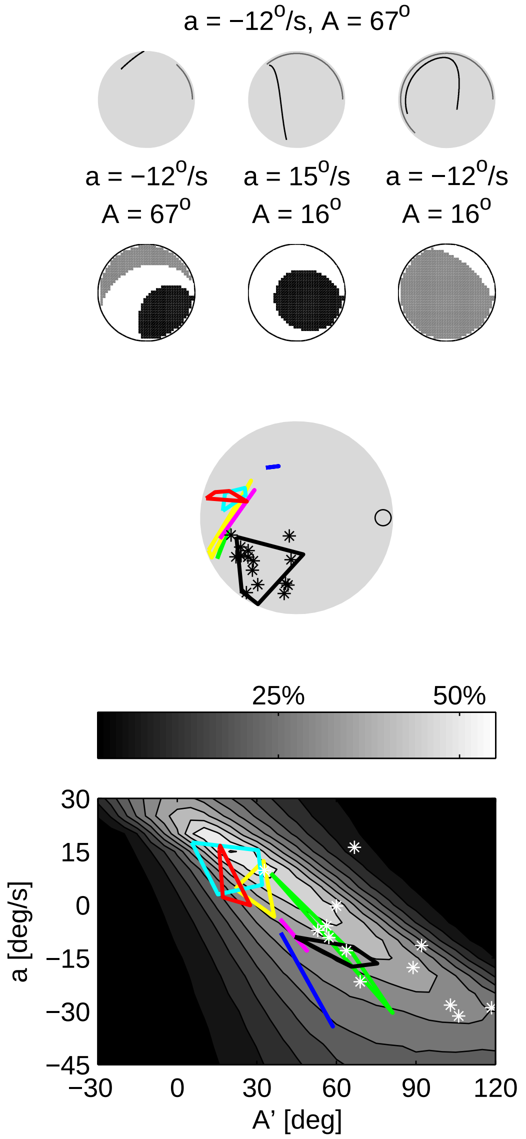


Figure 2.12.2: *An example of computational modelling of navigation towards moving target. Upper: Three different situations, in which subject navigates toward the moving target with value of the angle α (A) and its fixed change during the time (a). In this case, the most effective strategy is to start with a value 16° of α and increase it continuously at the rate of 15°/s. For each of three presented situations, is it possible to start from different locations inside the environment. Optimal array, from which animals could navigate toward the target, is shown by white color. Black color denotes the locations, from which it is impossible to catch the target. Trajectory of the target lines around the border of the arena. Trajectory of the virtual rat is drawn by darker line. Middle: Real locations, from which rats started to navigate towards the moving target. Each color represents a start position of one animal. Start position of the target is denoted by a blue circle on the right side. Lower: Plot of the relationship between the (A) and (a) for each animal. In general, empirical starting positions are in accordance with the proposed model. When animals had started with high value of (A), their value of (a) was negative. If animals started with lower or negative value of (A), (a) was positive. Adapted from Blahna and Klement, 2008.*

Part VIII

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Part IX

Manuscripts