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Spatial radial maze procedures and setups to dissociate local and distal relational spatial frameworks in humans

Léa Bertholet[a,b,*], Manuel Torres Escobar[b], Marion Depré[d], Camille F. Chavan[a], Fabienne Giuliani[c], Pascale Gisquet-Verrier[d], Delphine Preissmann[a,b], Françoise Schenk[a,b]

[a] *Institute of Psychology, University of Lausanne, CH-1005 Lausanne, Switzerland*
[b] *Center for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University, Hospital, CH-1008 Prilly, Switzerland*
[c] *Consultation of Liaison Psychiatry for Intellectual Disability, Community Psychiatry Service, Department of Psychiatry, University Hospital Center and University of Lausanne, Lausanne, Switzerland*
[d] *Institut des Neurosciences Paris-Saclay, UMR 9197/CNRS, Département Cognition & Comportement, Université Paris-Sud, Orsay F-91405, France*

HIGHLIGHTS

- Radial maze tasks in real and virtual environment adapted for humans.
- Enables control and dissociation of local and relational distal cues.
- Assessment of long-term and short-term memory for places.
- Flexible devices and procedures easily adapted for different subjects.
- In our mazes, the relative weight of local and distal cues revealed gender effect.

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ABSTRACT

Background: Radial maze tasks have been used to assess optimal foraging and spatial abilities in rodents. The spatial performance was based on a capacity to rely on a configuration of local and distant cues. We adapted maze procedures assessing the relative weight of local cues and distant landmarks for arm choice in humans.

New method: The procedure allowed testing memory of places in four experimental setups: a fingertip texture-groove maze, a tactile screen maze, a virtual radial maze and a walking size maze. During training, the four reinforced positions remained fixed relative to local and distal cues. During subsequent conflict trials, these frameworks were made conflictive in the prediction of reward locations.

Results: Three experiments showed that the relative weight of local and distal relational cues is affected by different factors such as cues' nature, visual access to the environment, real vs. virtual environment, and gender. A fourth experiment illustrated how a walking maze can be used with people suffering intellectual disability.

Comparison with existing methods: In our procedure, long-term (reference) and short-term (working) memory can be assessed. It is the first radial task adapted to human that enables dissociating local and distal cues, to provides an indication as to their relative salience. Our mazes are moveable and easily used in limited spaces. Tasks are performed with realistic and spontaneous though controlled exploratory movements.

Conclusion: Our tasks enabled highlighting the use of different strategies. In a clinical perspective, considering the use of compensatory strategies should orient towards adapted behavioural rehabilitation.

* Corresponding author at: Lausanne University, Hospital, Center for Psychiatric Neuroscience, Department of Psychiatry, bâtiment Albatros, 1008 Prilly, Switzerland. Tel.: +41 77 2101946; fax: +41 21 643 65 62.
E-mail address: Lea.Bertholet@gmail.com (L. Bertholet).

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1. Introduction

Spatial cognition relies on mental representations. Basically, however, it does *not refer to pictures in the head* but to *plans for obtaining* (and coding) *information from potential environments* (Neisser, 1976). Hence, spatial maps mediate anticipation assessed from decisions and actions in nonhuman species as well. They require the integration of polymodal (proprioceptive, vestibular, visual, auditory, etc) sensory information up to abstract representation. In animals, this process is based on the classical mechanism of path integration, from which the ongoing position is computed relative to the start of the journey (Etienne et al., 1996). The combination of information from proprioception with anticipation of movement decisions (i.e., the classical efferent copy) maintains a sense of being oriented and situated when exploring an environment. We have proposed that cognitive mapping requires the merging of bearing maps (anticipation of differential sensations during movement in a particular direction) with the assembly of local information in topographic sketch maps (Jacobs and Schenk, 2003). This allows to anticipate possible events (Kveraga et al., 2007; Schenk et al., 2007).

The historical and provocative proposition that the hippocampus, a large limbic structure, was involved in the elaboration of *cognitive maps* in rats and humans (O'Keefe and Nadel, 1978) has induced a vast amount of studies targeting the hippocampus and spatial memory using well thought out experimental procedures. These were mainly derived from short cut and detour experiments in conditions where *part* of the sensory information from the known environment was not no longer available. As predicted, it appeared that some pyramidal hippocampal neurons active in a spatial position did *not* require the availability of all the original sensory information to maintain stable spatial firing (O'Keefe and Conway, 1978; O'Keefe and Speakman, 1987). This provided the first indications that hippocampal pyramidal cells were *place units*, involved in a network activating a representation of the spatial relations between different cues in the environment. Later on, the involvement of the hippocampus in spatial orientation processes was confirmed in humans (Berthoz, 1997; Mellet et al., 2000; Burgess et al., 2002; Iglói et al., 2010).

In the late 1970s already, the "cognitive map hypothesis" led to the development of two elegant and simple tests assessing basic spatial memory properties in rats: the discrimination of a position relative to distant environment cues (a place) and the capacity to reach and remember multiple positions without retracing.

One design, the Morris maze (1981), was a large circular open field filled with water, with no local cue and an escape platform where rats were highly motivated to land (Schenk, 1998). Tasks based on this design were adapted for humans. Some were realistic walking tasks (Overman et al., 1996; Bohbot et al., 2002; Laczó et al., 2009; Bullens et al., 2010; Newman and Kaszniak, 2010; Majerová et al., 2012; Gazova et al., 2013). More often, they were embedded in virtual reality designs (Sandstrom et al., 1998; Astur et al., 2004; Hamilton et al., 2009; Barkas et al., 2010; Woolley et al., 2010; Chamizo et al., 2011; Livingstone-Lee et al., 2011, 2014; Van Gerven et al., 2012; Laczó et al., 2012; Fajnerová et al., 2014; Sneider et al., 2015).

The second task was performed in a radial maze encouraging spontaneous foraging in 8 or more different food sources before re-entering any one (Olton and Samuelson, 1976). This type of task can reveal strategy planning. It is also called elimination task because it is mediated by the memory of a series of visited places. Here, the cognitive load combines long-term place memory of each source with a short-term memory of the recently visited positions. It differs from the "traveling salesman problem" in that a central choice point restricted the cognitive load to the selection of 8 discrete directions. Both proactive and retrospective forms of memory are required in the free task performance (Cook et al., 1985; Kesner and DeSpain, 1988). Results obtained in specific maze designs suggested that rats can decide which alley to visit next when still in one arm extremity – rather than in the maze crossroad – as if relying on a global representation (Schenk et al., 1997). Finally, a special procedure was developed, in which local olfactory arm cues and distant spatial room cues predicted reinforcement during training (Lavenex and Schenk, 1996; Grandchamp and Schenk, 2006). In this design, a dissociation of these two reference frameworks by maze rotation (preserving the internal configuration) or by arm translation (internal disorganization) allowed to assess the relative weight of local and spatial cues for arm selection. This work revealed the surprisingly low priority of arm olfactory cues over spatial room cues for rats, especially when the apparatus was illuminated. It revealed thus that arm selection is preferentially based upon an integrated spatial global representation rather than on a list of separately identified items. The reliance on such spatial representation was reduced in aged rats and compensated by what seemed to be a more local selection strategy (Grandchamp and Schenk, 2006). Thus, only a dissociation procedure revealed the underlying change in aged rats, since the overall efficiency in arm patrolling was not reduced by age in this case. This suggested that a memory of specific and independent arm cues could help in compensating for a spatial strategy based on a global representation.

This later type of task thus has many advantages. It combines memory and executive functions and has been widely used in the rat to deal with brain structures involved in these mechanisms. A procedure dissociating local and distant cues is easy to design in order to sort out whether different populations of subjects favour local or global reference for arm choice. It is certainly easy to adapt task procedures for testing human subjects of different ages, gender or neurological status. Finding out which reference framework is favoured (if any) in a given population or individual can also help in rehabilitation approaches.

Elimination tasks developed for animals have been adapted for humans, whether realistic (Elmes, 1988; Overman et al., 1996; Abrahams et al., 1997, 1999; Glassman et al., 1998; Bohbot et al., 2002; Pentland et al., 2003; Rahman et al., 2005; Leitner et al., 2005; Mandolesi et al., 2009b; Girard et al., 2010; Palermo et al., 2014; Mennenga et al., 2014) or using virtual reality (Iaria et al., 2003; Astur et al., 2004, 2005; Bohbot et al., 2004, 2007, 2012; Levy et al., 2005; Etchamendy and Bohbot, 2007; Goodrich-Hunsaker and Hopkins, 2010; Banner et al., 2011; Andersen et al., 2012; Spieker et al., 2012; Etchamendy et al., 2012; Konishi and Bohbot, 2013; Wilkins et al., 2013). Among these studies only few used a radial task where only part of the arms were baited, and none presented a procedure dissociating local and distal cues. Some tasks were conducted in real environments (Elmes, 1988; Abrahams et al., 1997, 1999; Pentland et al., 2003; Rahman et al., 2005; Girard et al., 2010) and others in virtual environments (Astur et al., 2004, 2005; Levy et al., 2005; Goodrich-Hunsaker and Hopkins, 2010; Banner et al., 2011; Etchamendy et al., 2012; Spieker et al., 2012; Konishi and Bohbot, 2013).

We built different radial mazes in which the integration of body movements was required: following grooves with the fingertip or walking along floor alleys, sliding a finger on a tactile screen along alleys marked with colours or black and white patterns. For comparison, we developed a virtual screen maze driven with the direction arrows of the keyboard.

A general design, common to the different mazes, consisted in learning upon first visit that only 4 arms out of 8 were "reinforced" by a local event. Subjects had thus to develop a stable spatial memory to select the baited arms while relying on working memory to avoid re-entries. During this first phase, two spatial reference sets were predicting the baited positions. One was the global spatial framework relating subjects' movements and position with the