CHAPTER

5

Methodological Approaches to the Behavioural Investigation of Visual Perception in Rodents

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1. INTRODUCTION

Vision is the main sensory modality used by humans to acquire information about the environment and interact with the objects it contains. Our ability to extract from visual scenes, in a fraction of a second, key properties that guide our behaviour (Potter, 1976; Intraub, 1980; Thorpe et al., 1996; Keysers et al., 2001; Rousselet et al., 2002) is likely unparalleled both in the organic and artificial worlds — but see recent advances in machine vision systems based on convolutional neuronal networks (LeCun et al., 2015). Thus, it is not surprising that human visual perception has been the object of intense investigation since the times of Gestalt psychology (Wagemans et al., 2012a,b). At the same time, the need of understanding the neuronal underpinnings of visual cognition has promoted the use of various animal species as models of visual perception, so as to allow the application of invasive approaches to study the visual system (e.g., single- and multielectrode recordings, lesions as well as pharmacological and genetic manipulations).

Rodents were initially explored as models of visual functions by the pioneering studies of Karl Lashley (1930a,b, 1938) and contemporaries (Munn, 1930; Fields, 1932, 1935, 1936; Krechevsky, 1938a,b) at the beginning of the previous century (see Zoccolan, 2015 for a review) but were soon abandoned in favour of species with higher visual acuity, such as small carnivores, and closer evolutionary proximity to humans, such as nonhuman primates. The latter, in particular, have been the model of choice for experiments combining psychophysical tests of visual perception with invasive recordings and manipulations in visual cortex, given the amenability of monkeys to be trained in complex visual discrimination tasks and their similarities with humans in terms of overall brain organization, as well as structural and functional properties of the visual system (Maunsell and Newsome, 1987; Logothetis and Sheinberg, 1996; Tanaka, 1996; Rolls, 2000; Orban, 2008; Nassi and Callaway, 2009; Kourtzi and Connor, 2011; DiCarlo et al., 2012). Meanwhile, rodent vision was not completely ignored, but the use of rodent species was mainly confined to developmental studies of plasticity mechanisms in visual cortex (Berardi et al., 2000, 2003; Spolidoro et al., 2009; Espinosa and Stryker, 2012; Sale et al., 2014) and lesions studies targeting the anatomical substrates of object recognition memory (Brown and Aggleton, 2001; Bussey and Saksida, 2005, 2007; Murray et al., 2007; Squire et al., 2007).

Over the past 10 years, this trend started to reverse, thanks to a new wave of neurophysiological, anatomical, imaging and behavioural studies exploiting the experimental advantages of mice and rats in the investigation of visual functions — for a review, see Huberman and Niell (2011), Niell (2011), Katzner and Weigelt (2013), Carandini and Churchland (2013), Glickfeld et al. (2014), Gavornik and Bear (2014), Niell (2015), Reinagel (2015), Zoccolan (2015), Cooke and Bear (2015) and Glickfeld and Olsen (2017). On the neurophysiological and anatomical front, these studies have revealed how the visual cortex of rodents is organized in clusters of strongly reciprocally connected areas (Wang and Burkhalter, 2007; Wang et al., 2011, 2012), whose functions partially overlap with those of the visual pathways that, in primates, are specialized for the processing of shape and motion information (Andermann et al., 2011; Marshel et al., 2011; Vermaercke et al., 2014b; Juavinett and Callaway, 2015; Vinken et al., 2017; Tafazoli et al., 2017). Primary visual cortex, in turn, has been shown to contain distinct neuronal subpopulations that selectively

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route specific bands of spatiotemporal information to the abovementioned pathways (Gao et al., 2010; Glickfeld et al., 2013a; Ji et al., 2015). Given the powerful array of experimental approaches that are available in rodents, ranging from high-resolution two-photon imaging and in vivo whole-cell recordings (Margrie et al., 2002; Ohki et al., 2005; Lee et al., 2006; Greenberg et al., 2008; Pawlak et al., 2013) to molecular and genetic manipulations (Luo et al., 2008; Fenno et al., 2011; Deisseroth, 2011; Tye and Deisseroth, 2012; Kim et al., 2017), these findings bring the promise to dissect the neuronal computations underlying visual functions as advanced as shape and motion processing at the molecular, synaptic and circuitry levels − a goal that seems currently out of reach in primates.

At the same time, current investigations of visual cortical processing in rodents are limited by the fact that neurophysiological approaches are typically applied in animals that are not engaged in visual discrimination tasks. Most rodent studies are based on anesthetized or passively viewing subjects, either stationary or running over a treadmill or trackball (Niell and Stryker, 2008, 2010; Andermann et al., 2011; Marshel et al., 2011; Froudarakis et al., 2014; Vermaercke et al., 2014b; Juavinett and Callaway, 2015; Vinken et al., 2017; Tafazoli et al., 2017). This is not due to a lack of behavioural studies of rodent vision. Quite the opposite − several investigators have explored rodent visual functions at the behavioural level, showing, for instance, that rats are capable of advanced processing of visual object information (Zoccolan, 2015). In particular, they are able to recognize visual objects in spite of major changes in their appearance (Zoccolan et al., 2009; Tafazoli et al., 2012; Vermaercke and Op de Beeck, 2012; Vinken et al., 2014), a key feature of primate vision known as *transformation-tolerant* (or *invariant*) object recognition (DiCarlo et al., 2012), and they do so by integrating multiple shape features into their perceptual strategy (Alemi-Neissi et al., 2013; Rosselli et al., 2015). In other words, the behavioural evidence matches quite well with the neurophysiological one, but behavioural and functional studies of visual cortical processing are still rarely combined in rodents (see Cooke et al., 2015; Burgess et al., 2016b). This is a limitation, since a thorough understanding of the visual system will likely require a synergistic application of behavioural, neurophysiological, interventional and computational approaches (Panzeri et al., 2017; Jazayeri and Afraz, 2017). It is our opinion that such a limited integration of behavioural and neurophysiological procedures is partly due to the lack of a unified, consolidated knowledge, in the vision science community, about the behavioural methods that are available to study visual functions in rodents. The goal of this chapter is to carry out a survey of such methods, at the level of both experimental apparatus and task/stimulus design, thus providing a compendium of what is possible to achieve in the investigation of rodent visual behaviour.

1.1 Organization of the Chapter

A very large variety of behavioural approaches have been developed to probe rodent vision, possibly larger than in the case of primates. Monkeys are typically tested with the body restrained in apposite chairs and the head held stationary through head fixation. This allows a very good control of basic properties of the visual stimuli (such as retinal size and position, when eye tracking is also applied). In addition, monkeys are usually trained to explicitly report the identity of a set of visual stimuli, by either pressing a lever or making saccades to specific target locations over the stimulus display (more rarely, by directly touching the target stimuli on the display). By contrast, rodents have been often tested under fully unrestrained conditions, free to approach and explore the visual stimuli, consisting, in many cases, of solid objects. Such free explorations often do not require an explicit recognition of trained stimuli but relay on the spontaneous preference of rats and mice for novel, less familiar objects. Only recently, behavioural rigs have been developed that are more similar to those used in monkey studies, with the body and the head of the rodent being fully or partially restrained, and explicit responses being collected through licking sensors placed near to the animal's mouth (Zoccolan, 2015).

To present such a variety of methods in a reader-friendly way, we have divided rodent behavioural studies into two major categories: (1) those that exploit innate preferences or spontaneous reactions of the animals towards visual stimuli to implicitly measure their perceptual choices (Section 2); and (2) those that require training the animals in visual discrimination tasks and instructing them to explicitly report their perceptual decisions (Section 3). For both classes of approaches, we have further organized the literature along two main methodological axes: (1) task/stimulus design; and (2) training/testing apparatus.

The first axis is used to map visual tasks according to (1) the number of stimuli an animal is simultaneously presented with; and (2) the number of alternative responses the animal is allowed to provide. For instance, in the case of the first class of studies (i.e., those relying on implicit responses), we treat separately the tasks based on spontaneous object recognition (where two objects are presented in each session and two exploration times are measured), and the tasks where a single stimulus is used to elicit an innate behaviour (e.g., freezing or fleeing). In the case of the second class of studies (i.e., those relying on collection of explicit responses), we distinguish between designs in which a

single stimulus is shown to an animal and a single response is acquired (as in the Go/No-Go task), and designs where two stimuli are simultaneously presented to the animal and two possible responses are allowed (as in two-alternative forced choice tasks). With regard to the second methodological axis, we have classified the behavioural rigs used to test rodent vision depending on the extent to which the animal is allowed to freely interact with the environment, i.e., according to whether is freely moving, partially restrained, head-fixed or head-fixed in a virtual reality rig (e.g., trackball). Tables 5.1 and 5.2 summarize how the literature about rodent visual behaviour is distributed in the two classes of studies based, respectively, on implicit and explicit tests, and across the possible combinations of experimental design and apparatus.

Finally, the last section of the chapter (Section 4) presents an overview of some of the most advanced psychophysical procedures that have been recently applied to investigate rodent visual perception. These approaches (such as visual priming and classification image paradigms) are derived from well-established methods to study visual processing in primates and illustrate how the field of rodent visual perception has been rapidly evolving to reach methodological standards not dissimilar from those of human and monkey studies.

2. APPROACHES BASED ON COLLECTION OF SPONTANEOUS RESPONSES

2.1 Tests of Spontaneous Object Recognition

The tests of Spontaneous Object Recognition (SOR) are the most popular approaches to probe recognition memory in rodents (Ennaceur, 2010; Antunes and Biala, 2012; Cohen and Stackman, 2015; Grayson et al., 2015; Kinnavane et al., 2015; Blaser and Heyser, 2015). Their main field of application is as a tool to locate the neuroanatomical substrates of the memory-formation processes underlying object recognition. As such, they are often paired to interventional approaches, such as mechanical or pharmacological lesions, to causally test the involvement of specific brain regions in object recognition memory − for recent examples, see Clark et al. (2000), Astur et al. (2002), Gaskin et al. (2003), Mumby et al. (2005), Ainge et al. (2006), Dere et al. (2007) and Hughes (2007).

The SOR test was originally developed in rodents as an adaptation of the delayed-non-match-to-sample test (DNMS), used with the same purpose in primates and humans (Mishkin and Delacour, 1975; Eacott et al., 1994; Holdstock et al., 2000). SOR and DNMS tasks usually give comparable results in rodents, but they engage different types of encoding: passive and spontaneous in the first case; active and forced in the second one. Method-wise, while DNMS tasks require long and laborious training procedures and pose several challenges in terms of attaining the desired criterion performances from rodent subjects (Aggleton, 1985; Mumby et al., 1990; Steckler et al., 1998; Prusky et al., 2004b), SOR tests are not only more readily implementable (since they do not involve motivational manipulations and explicit training) but they are also more sensitive to memory impairment and they yield results that are highly consistent across species (Nemanic et al., 2004; Clark and Martin, 2005; Clark and Squire, 2010).

The SOR task exploits rodent innate preference towards novelty as a measure of recognition: longer exploration of a novel object over a familiar one is interpreted as implicit recognition (and thus former memorization) of the familiar object (Ennaceur, 2010). The SOR task is also called Novel Object Preference test (NOP) or Novel Object Recognition test (NOR). While the first definition correctly captures the essence of the task, since the preference for a novel object implies the concomitant recognition of a familiar one, the second definition is semantically incorrect − recognition requires a prior exposure to the object, which is not possible if the object is novel. To avoid confusion, we consistently use the term SOR, throughout the chapter, to refer to this test.

A standard SOR task typically consists of two different phases (Besheer and Bevins, 2006). First, there is a sample session, where the rodent is exposed to two identical copies of a novel object in a familiar arena. The memory of the object is encoded during this phase, when the animal explores the two items. After a variable delay, a test session follows, where the rodent is exposed to a third replica of the familiar object, presented along with a novel one. The test of object memory retrieval takes place when the animal explores these two items. Usually, no feedback (e.g., reward) is provided to the subject during the task.

In general, laboratory mice and rats exhibit an innate tendency to explore objects, especially when they are unfamiliar (Barnett, 2007). Thus, object memory strength is inferred from the time spent by the animal exploring the novel object over the familiar one during the test session. Object exploration time is typically quantified by measuring how long the animal stays in close proximity to the object, with its snout directed to it. The exploration times of the two objects are then combined to yield either a *novel object preference ratio*, with the time devoted to explore the novel object divided by the total exploration time, or a *discrimination ratio*, with the difference between the times spent to explore the novel and unfamiliar objects divided by the total exploration time.

TABLE 5.1 Studies Based on Collection of Spontaneous Responses

Spontaneous Object Recognition	Spontaneous Responses in Ethological Contexts	Navigation in Virtual Environments
Aggleton 1997 – R	Cooke 2015 – M	Aronov 2014 – R
Albasser 2009, 2010a, 2010b, 2011 – R	De Franceschi 2016 – M	Cushman 2013 – R
Amen-Ali 2012, 2015 – R	Hoy 2016 – M	Hölscher 2005 – R
Antunes 2012 – M/R	Sawinskia 2009 – R	Lee 2007 – R
Barker 2007 – R	Vale 2017 – M	Chen 2013 – M
Bartko 2007 – R	Vinken 2017 – R	Dombeck 2010 – M
Bartko 2007a, 2007b – R	Wallace 2013 – R	Domnisoru 2013 – M
Bevins 2006 – R/M	Wei 2015 – M	Fiser 2016 – M
Blaser 2015	Yilmaz 2013 – M	Harvey 2009, 2012 – M
Braida 2013 – M	Zhao 2014 – M	Keller 2012 – M
Broadbent 2010 – R		Saleem 2013 – M
Burke 2015 – R/M		Schmidt-Hieber 2013 – M
Bussey 2000 – R		Youngstrom 2012 – M
Clark 2000 – R		Zmarz 2016 – M
Clark 2011 – R		
Cloke 2015 – R/M		
Cohen 2013 – M		
Cohen 2015 – R/M		
Dix 1999 – R		
Dudchenko 2004 – R/M		
Eacott 2004 – R		
Ennaceur 1988, 1996, 1997, 2004, 2009 – R		
Ennaceur 2010 – R/M		
Forwood 2005, 2007 – R		
Gaskin 2010 – R		
Heyser 2012 – M		
Heyser 2013 – R		
Kinnavane 2015 – R/M		
Langston 2010 – R		
Lyon 2012 – R/M		
Mumby 2001, 2002, 2005 – R		
Norman 2004, 2005 – R		
Powell 2004 – M		
Prickaerts 2005 – R		
Reid 2012, 2014 – R		
Romberg 2014 – R		
Sambeth 2007 – R		
Sieben 2015 – R		
Vasconcelos 2011 – R		
Winters 2004, 2005a, 2005b, 2006, 2008, 2010 – R		

The table reports the studies referenced in the chapter that are based on collection of spontaneous responses. The letters R and M refer to studies testing, respectively, rats and mice. The shades of grey in the cells specify the level of control over the position of the head/body of the animals; *light grey*: freely moving; *darker grey*: partially restricted; *very dark grey*: head-fixed.

TABLE 5.2 Studies Based on Explicitly Training Rodents in Visual Discrimination Tasks

One Stimulus – One Choice	Two Stimuli – Two Choices	One Stimulus – Two Choices
Dean 1981	Brooks 2013 – R	Bussey 1997 – R
Kurylo 2015, 2017 – R	Bari 2009 – R	Gleiss 2012 – R
Lee 2016 – R	Birch 1979 – R	Meier 2011, 2013 – R
Andermann 2010 – M	Bossens 2016 – R/H	Petruno 2013 – R
Bennett 2013 – M	Botly 2012 – R	Raposo 2012 – R/H
Berditchevskaia 2016 – M	Busse 2011 – M	Raposo 2014 – R
Glickfeld 2013b – M	Bussey 1997b – R	Reinagel 2013 – R
Goard 2016 – M	Bussey 2008 – R	Sheppard 2013 – M
Guo 2014 – M	Carlsson 2010 – R	Siemann 2015 – M
Histed 2012 – M	Clark 2011 – R	Alemi-Neissi 2013 – R
Khastkhodaei 2016 – M	Cook 2004 – R	Bussey 1997a – R
Lee 2012 – M	Davies 2007 – R	Hirokawa 2008 – R
Long 2015 – M	De Keyser 2015 – R	Kurylo 1997, 2008a, 2008b – R
Makino 2015 – M	Douglas 2006 – R/M	Odoemene 2017 – M
Montijn 2015 – M	Driscoll 2005 – R	Rosselli 2015 – R
Pinto 2013 – M	Eacott 2001, 2003 – R	Sakata 2004 – R
Schwarz 2010 – R	Gaffan 1995, 1996, 2000, 2001, 2004 – R	Tafazoli 2012 – R
	Iversen 1993 – R	Zoccolan 2009 – R
	Keller 2000 – R	Burgess 2016a – M
	Long 2015 – M	Scott 2013, 2015 – R
	Mar 2013 – R/M	
	Mar 2013 – R/M	
	Meier 2011, 2013 – R	
	Minini 2006 – R	
	Petruno 2013 – R	
	Pinto-Hamuy 1987 – R	
	Prusky 2000a,b, 2002, 2003, 2004 – R/M	
	Reinagel 2015 – R	
	Romberg 2013 – M	
	Simpson 1999 – R	
	Stirman 2016 – M	
	Sutherland 1961, 1962a, 1962b, 1969 – R	
	Vermaercke 2012, 2014a, 2015 – R/H	
	Vinken 2014 – R	
	Wiesenfeld 1976 – R	
	Fields 1932, 1935, 1936 – R	
	Krechevsky 1938a, 1938b – R	
	Lashley 1930a, 1930b, 1938 – R	
	Munn 1930 – R	
	Burgess 2016a – M	

The table reports the studies referenced in the chapter that are based on explicitly training rodents in visual discrimination tasks. The letters R, M and H refer to studies testing, respectively, rats, mice and humans. The shades of grey in the cells specify the level of control over the position of the head/body of the animals; *light grey*: freely moving; *darker grey*: partially restricted; *very dark grey*: head-fixed.

As previously mentioned, the goal of most SOR studies is to identify the brain structures, such as hippocampus and perirhinal cortex, underlying the encoding and retrieval of object memory. Traditionally, no much care was taken to ensure that these processes were exclusively mediated through a specific sensory modality. The use of solid 'junk' objects allowed the animals to freely explore the items using vision, touch and smell (Antunes and Biala, 2012; Blaser and Heyser, 2015). More recently, several investigators have restricted the access to the objects through specific senses only, with the goal of testing whether encoding of object memory in a given modality (e.g., visual) allows retrieval in a different one (e.g., tactile), as in cross-modal SOR tasks (Forwood et al., 2007; Albasser et al., 2010b, 2011; Winters and Reid, 2010; Reid et al., 2012, 2014). Nevertheless, from the point of view of probing visual perception, the use of solid objects makes it extremely difficult to infer what visual features an animal may be sensitive to in a given SOR task — shape, brightness, colour, texture or any combination of these features, along with possible (uncontrolled) contributions from other modalities (e.g., odours), may be used by the subject to discriminate the objects.

Yet, till recently, SOR tasks have been the more widely applied tools to investigate object recognition in rodents, owing to the many experimental advantages they afford. First, because the rule is spontaneous, acquisition of the task is virtually immediate and without the need of any training (apart from an initial habituation to the experimental rig). Second, several key experimental factors, such as task difficulty or the brain structures involved in the encoding and retrieval processes, may be changed simply by altering the length of the interval between the sample and test sessions (Cohen and Stackman, 2015). Third, in its simpler form, the task does not require any external motivation, reward or punishment. Finally, recognition memory of objects in specific spatial locations or context may also be concomitantly tested (Dix and Aggleton, 1999; Eacott and Norman, 2004; Norman and Eacott, 2005; Langston and Wood, 2010).

Recently, however, some authors have pointed out several limitations of SOR tasks, in an effort to explain the contradictory results often obtained across studies of object recognition memory in rodents (Ennaceur, 2010; Cohen and Stackman, 2015; Kinnavane et al., 2015; Blaser and Heyser, 2015). In fact, the features that make SOR tasks so popular, as the ease of training and testing, are also potentially responsible of inconsistences among studies — especially because there is considerable variability, across laboratories, in the implementation of SOR tasks.

2.1.1 Limitations of Standard Spontaneous Object Recognition Tasks

To start, the spontaneous nature of the task produces substantial inter-animal variance, thus decreasing the statistical power of the test. The lack of any common, strong external motivation across rats (like water or food deprivation) implies that the subjects only act out of curiosity, leaving room for idiosyncratic preferences towards the objects. The inter-subject variance can be further enhanced by the reaction of each individual animal to unfamiliar features of the arena and to the frequent handling between trials (Powell et al., 2004; Ennaceur et al., 2009). Both factors can increase the stress level of the subjects, making them neophobic and thus interfering with the behaviour upon which the whole experimental design rests — the spontaneous drive towards novel objects.

With regard to the stimuli, there is no standard set of objects that is consistently used across studies and laboratories. More importantly, little attention is usually paid to the perceptual properties that could potentially make an object more salient and attractive than another one, regardless of its novelty. This issue is exacerbated by the fact that the animals are typically free to interact with solid objects through multiple sensory modalities. Among the sensory features that can act as potential confounds in SOR tasks, only odour differences are systematically and effectively avoided, by using triplets of junk objects and cleaning them between sessions. By contrast, the visual properties of the stimuli are rarely controlled or even mentioned in SOR studies, possibly because, until recently, visual perception has been largely underestimated in rodents. This is a potentially serious issue because accumulating behavioural and neurophysiological evidence suggests that rodents are capable of rather advanced processing of visual object information (Zoccolan, 2015; Tafazoli et al., 2017). Therefore, it is possible that rats and mice perceive different objects as more or less attractive or repulsive (or even safe or dangerous) because of their shape, colour or brightness. Moreover, even though the familiar object is the same in the sample and test sessions, its pose (and, therefore, its appearance) slightly changes in an uncontrolled way from trial to trial, as a function of the specific direction chosen by the animal to approach the item. Several studies have shown that rat recognition is only partially tolerant to such view changes (Zoccolan et al., 2009; Alemi-Neissi et al., 2013; Rosselli et al., 2015), thus raising the question of how 'novel' a familiar object may appear under a different pose, as compared to a truly novel object. Also tactile perception is rarely taken into account when designing SOR studies, as the structure and texture of the objects is typically not controlled. This leaves open the possibility that objects with more protrusions and/or intrusions are more perceivable and offer larger affordance than smooth objects. For instance, rats were found to preferentially explore objects they could climb onto, as compared to those they could not (Chemero and Heyser, 2005; Heyser and Chemero, 2012).

In summary, the lack of control over the visual and haptic attributes of the stimuli can be a major source of confound and possibly lead to inconsistent results among studies relying on different sets of objects.

In terms of testing procedures, there is no agreed-upon standard among laboratories on how to correctly measure whether an exploration bout is taking place, apart from recording the position of the animal in the arena or the direction of his snout. These analyses are either automatized, through the application of a tracking software (Romberg et al., 2013; Cohen et al., 2013; Sieben et al., 2015), or are performed manually by the investigators, through visual inspection of rat behaviour with the aid of apposite computer programs (Winters et al., 2004, 2006; Forwood et al., 2007; Bartko et al., 2007a; Barker et al., 2007; Albasser et al., 2009, 2011, 2010b; Winters and Reid, 2010; Ameen-Ali et al., 2012; Reid et al., 2014) or a simple stopwatch (Heyser and Chemero, 2012; Braida et al., 2013; Heyser and Ferris, 2013) − experimenters are generally blind to the treatment conditions of each rat. Obviously, the use of automated tracking procedures guarantees more objective scores, as well as better inter-trial and inter-animal uniformity of judgement. Another issue is the fact that very few trials per day can be collected (usually it takes 7−10 min per trial per rat) because of the need to manually replace the objects in the arena and the extensive handling of the animals in between trials. Yet another source of possible inconsistencies across studies is the variable duration of object exploration during the sample session, which typically lasts between 3 and 5 min (Ennaceur et al., 1996; Aggleton et al., 1997; Ennaceur and Aggleton, 1997; Mumby et al., 2002, 2005; Albasser et al., 2009; Broadbent et al., 2010; Gaskin et al., 2010). Such variability can affect the encoding, consolidation and retrieval of the memory of the familiar object − items explored for a longer time during the sample phase will be more readily recognized as familiar in the test session, thus sensibly influencing the outcome of the SOR test (Dix and Aggleton, 1999; Albasser et al., 2009). According to Kinnavane et al. (2015), imposing a rigid constraint on the duration of object exploration in the sample session is essential for properly interpreting the results of the test session, within and between studies. Recently, this led several authors to use a procedure where the sample session is ended once the rodent has explored the object for a certain amount of time − e.g., between 15 and 40 s (Aggleton et al., 1997; Ennaceur and Aggleton, 1997; Bussey et al., 2000; Clark et al., 2000; Winters et al., 2004; Forwood et al., 2005). While this approach certainly improves the control over the information that the animals are able to extract from the objects, caution should be taken when imposing a fixed exploration time across objects spanning a wide range of perceptual properties. In fact, object recognition, in rodents, depends on the visual/structural complexity of the target objects (Rosselli et al., 2015), and a hard constraint that does not take into account possible differences among the objects in terms of featural complexity may still not guarantee that all the objects within an experiment are sampled and encoded equally well during the process of memory formation.

In general, given the number of different factors that may tamper with the consistency and reproducibility of the results within and between studies, it is important to statically assess not only the difference between the discrimination or preference ratios obtained for the control (or sham) and experimental (or treatment) groups but also whether each group significantly differs from chance. As pointed out in a recent review (Cohen and Stackman, 2015), such additional test is not systematically carried out in SOR studies. This can lead to misinterpretations, especially in cases where the control group does not show a significant preference for the novel object, thus questioning the validity of the whole recognition memory test.

2.1.2 *Improved Variants of Spontaneous Object Recognition Tasks*

Because of the limitations reviewed above, several investigators have tried to improve the SOR task, although most efforts have been devoted not much to standardize the stimuli and the procedure but to ameliorate the experimental rig. The SOR task was originally conceived to test object recognition memory inside a square arena because it was the easiest way to test and measure a subject's behaviour. Only recently, several authors have started to develop and use different experimental layouts, such as the Y-maze (Winters et al., 2004, 2008; Forwood et al., 2005; Bartko et al., 2007a,b), the E-maze (Ameen-Ali et al., 2012) or the bow-tie maze (Albasser et al., 2010b).

In the Y-maze, the base of the Y is used as the starting arm, while the two arms stemming from the bifurcation are used both to place the identical copies of the objects during the sample phase and then for placing familiar and novel objects during the test phase. Thanks to this design, it is possible to better control stimulus appearance, always presenting to the animal, in each trial, the same side of the objects. Moreover, the animals have less space to wander around and are closer to the stimuli − this increases the level of exploration and makes its assessment easier. Finally, the Y-maze makes it easier to restrict the test of recognition memory to single sensory modalities. Purely visual sensing is enforced by blocking the access to the objects with transparent panels, while purely tactile exploration is achieved by presenting them in the dark. This design was essential for testing cross-modal memorization and recognition in some recent SOR studies (Winters and Reid, 2010; Reid et al., 2014).

The bow-tie maze introduced by Albasser et al. (2010a,b, 2011) was designed as a hybrid between a DNMS and a SOR task, so as to exploit the advantages of the latter, while correcting some of its shortcomings. The maze is shaped as a bow-tie, with pairs of objects on each side, and a sliding door in the middle that separates the two ends of the maze. This makes it possible to have discrete trials and minimize the need for the investigators to handle the rodent subjects. In the standard application of this test (known as *running recognition*), during the very first trial, the animal explores a single object located at one side of the maze (sample phase). The rodent then moves to the other side of the maze, where is presented with a copy of the previously encountered object, along with a novel object (test phase). The latter becomes the familiar object for the test phase of the next trial, when the animal moves back to the other side of the maze. The task proceeds following this alternation, with each novel object encountered by the animal becoming the familiar object for the successive trial. In this way, the arrival arm of a trial becomes the starting arm of the next one, thus allowing multiple test trials within a single session. Food rewards are placed under both the objects in each arm, so as to increase the motivation of the animal, while, at the same time, avoiding the need of training an explicit matching rule. The trial duration is typically constrained to 1 min. Such limited exploration time, during both the sample and test phases, does not affect the validity of the results, because, during SOR tasks, the most discriminatory exploration bout takes place at the beginning of each session (Dix and Aggleton, 1999).

Using the bow-tie maze, it is possible to administer six trials in the time that is typically required to administer one trial in a standard SOR task. One could wonder, however, how this new protocol compares to the traditional SOR task in terms of achieved recognition memory, since the animal may not be able to exhaustively explore the novel object, so as to turn it into a familiar one for the next trial, given the overall speed of the procedure. This question was addressed by Ameen-Ali et al. (2012) in one of the phases of development of their E-maze. This new behavioural protocol can be considered as another improvement of the traditional SOR task, where features of the DNMS task are integrated in the task design (as in the case of the bow-tie maze). The apparatus is similar to a Y-maze, but with external passages connecting the object area to the holding area. The rodent moves continuously between these two areas to explore the objects and retrieve a reward, in a similar way to the running recognition protocol of Albasser et al. (2010). Compared to the bow-tie maze, having only one object area has the advantage that it is possible to have the same object placed in different positions or to change the context, so as to test, respectively, object-location and object-in-context memory. Critically, Amee-Ali et al. (2012) found no significant difference in recognition memory for animals tested in the same E-maze, but using either a traditional SOR protocol (with distinct, alternating sample and test phases) or a running protocol, similar to the one used by Albasser et al. (2010) in the bow-tie maze (with the current test phase becoming the sample phase for the next trial). Thus, regardless of the specific type of apparatus being used (bow-tie or E-maze), the possibility of having a continuous sequence of trials, with the same objects used both as novel and familiar (and all rewarded), addresses two of the main disadvantages of the traditional SOR task: (1) it increases the amount of data collected per session; and (2) it reduces the confounds produced by possible differences between novel and familiar objects in terms of perceptual complexity and affordances (see previous section).

Some authors have also succeeded in replacing the 3-dimensional (3D) objects commonly used in SOR studies with 2-dimensional (2D) stimuli (Forwood et al., 2007; Romberg et al., 2013; Braida et al., 2013). This not only allows restricting stimulus presentation to the visual modality only, thus isolating the contribution of visual perception to the encoding of object memories, but also allows matching the objects along several dimensions, such as shape, brightness and size. On the other hand, limiting the available information to the visual modality reduces the time rodents devolve to explore the stimuli and possibly their motivation in doing so.

Presentation of 2D stimuli in SOR tasks has been implemented in both rats and mice, using different rigs and experimental designs. Forwood et al. (2007) tested rats with both naturalistic and abstract images, placed at the end of the decision arms in a Y-maze. Specifically, the authors used (1) colour pictures of real 3D objects, tested in a previous SOR task, along with other photos; and (2) high-contrast shapes and textured patterns. The use of first class of stimuli led to two conclusions. First, novelty preference, and thus object memorization and recognition, is still present when 3D objects are replaced with their 2D pictures. Second, the use of image stimuli instead of real objects indeed reduces the total amount of exploration, during both the sample and test sessions. The use of the second class of stimuli revealed how the choice of the objects matters in terms of memorization — photos of real objects and textured patterns were recognized after a longer delay, compared to high-contrast shapes. This suggests that more complex visual stimuli likely produce richer perceptual representations, which, in turn, lead to the encoding of stronger memories. This finding also cautions against the use of simple high-contrast shapes in tests of object recognition memory (Bussey et al., 1997; Prusky et al., 2004b) because they can lead to an underestimation of rodent capabilities in such memory tasks (Forwood et al., 2007).

The other two studies employing 2D objects tested mice as subjects and relied on black-and-white images as stimuli. Braida et al. (2013) used a rectangular SOR arena, presenting either 3D objects (e.g., cylinders and LEGO assemblies) or showing simple geometrical shapes (e.g., triangles and squares) over two computer-controlled displays, placed on opposite walls of the arena. Both classes of stimuli yielded a comparable discrimination index. An unusual effort was made in this study to characterize the properties of the visual stimuli. The pairs of shapes presented to the mice were divided according to their discriminability, as assessed by their discrimination ratio. More importantly, the relationship between static and dynamic visual information was explored, by testing the highly discriminable and poorly discriminable stimuli while moving in various directions. The result was that mice were able to discriminate different motion directions independently from the shape. In addition, moving objects were better memorized than stationary ones, even when motion direction was the same for the two shapes in the sample and test sessions, thus showing that motion is a powerful cue in enhancing mice attention to the stimuli and consequent memorization. Finally, Romberg et al. (2013) tried to further develop the 2D variant of the SOR task as a part of a battery of cognitive tests. Their main innovation was the use of a touchscreen to assess rodent exploration, a device that is typically employed only in explicit tests of visual memory, cognition or perception (see Section 3.2). The touchscreen allows computing the discrimination ratio in a more precise and objective way, by measuring the amount of touches to the screen rather than the animal's exploration time. In addition, this procedure allows a tighter control over the visual appearance of the stimuli, compared to standard SOR studies — e.g., in Romberg et al. (2013), both the viewing distance and the brightness of the objects were matched.

2.2 Spontaneous Responses in Ethological Contexts

In addition to the spontaneous drive to explore novel objects, which is exploited in SOR tasks, other innate behaviours of laboratory mice and rats can be used to probe visual perception and, more in general, visual cognition in these species. These include navigation (e.g., for foraging), freezing, fleeing, hunting and visually driven reflexes, such as optokinetic responses.

Studies of spatial navigation typically do not investigate visual or, more in general, sensory processing per se, since they are mostly concerned with understanding how the location of the rodent in various kinds of environment is represented in hippocampus and parahippocampal areas, such as entorhinal cortex (Moser et al., 2008, 2015, 2017). Nevertheless, it has long been known that rats preferentially, although not exclusively, rely on visual cues when orienting and navigating through the environment (Zoladek and Roberts, 1978; Suzuki et al., 1980; Morris, 1981; Sutherland and Dyck, 1984; Schenk, 1985; Whishaw and Mittleman, 1986, 1986; Maaswinkel and Whishaw, 1999). The neuronal signature of this dependence of rodent spatial processing on vision has been found in the locking of hippocampal place fields to spatial visual landmarks and their remapping when such cues are changed (O'Keefe and Conway, 1978; Muller and Kubie, 1987; O'Keefe and Speakman, 1987; Gothard et al., 1996; Lee et al., 2004; Jezek et al., 2011), along with the influence of visual cues on hippocampal direction selectivity (Acharya et al., 2016). Typical navigation experiments, however, do not allow a precise control of the properties of the visual stimuli, given the (often) fully unconstrained nature of the experimental design. Only recently, with the advent of virtual reality mazes, where mice or rats are head-fixed and allowed to walk/run over a treadmill or a trackball, a better control of stimulus presentation has been achieved during navigation. This has opened up the possibility to investigate visual processing during semi-naturalistic and spontaneous exploration bouts. These studies will be reviewed in Section 2.3.

Among visually driven reflexes, the optokinetic nystagmus has been used, in both mice and rats, to measure visual acuity (Prusky et al., 2004a, 2008; Douglas et al., 2005) and investigate eye movements (Hess et al., 1985; Stahl et al., 2000; Stahl, 2004; Zoccolan et al., 2010). Such reflex, however, is mediated by subcortical structures and cannot be used to study visual cortical processing. More recently, another stereotyped motor response was used to obtain a spontaneous behavioural measure of stimulus detection, as well as contrast and spatial frequency sensitivity in mice (Cooke et al., 2015). The reflex consists in the visually induced fidget (named 'vidget' by the authors) of the forepaws of an awake, head-fixed mouse in response to the appearance of a phase-reversing sinusoidal grating stimulus (with the response recorded through a piezoelectric sensor). The advantage of measuring the vidget rather than the optokinetic reflex is the fact that the former requires processing in primary visual cortex (V1). This suggests the possibility of measuring the vidget, while simultaneously recording from V1 and other visual cortical areas, so as to link the detection of unexpected changes in the visual input (e.g., in terms of motion or shape content) to the underlying neuronal correlates across striate and extrastriate cortex (e.g., see Vinken et al., 2017).

Considering more complex behaviours, an interesting spontaneous response, as far as rodent visual perception is concerned, is the choice between flight and freeze, following presentation of a moving visual object, either above or

beside a laboratory rat or mouse. For instance, visual display of a looming black disc triggers an immediate flight or freeze response in mice (Yilmaz and Meister, 2013). This happens because this kind of stimulus resembles the visual input produced by a potential predator. Several studies have exploited this behaviour as a tool to investigate visual processing (Zhao et al., 2014; Wei et al., 2015; Vale et al., 2017). A few authors, in particular, have tried to better characterize the relationship between rodent defence strategies and the visual properties of the eliciting stimulus (Wallace et al., 2013; Yilmaz and Meister, 2013; De Franceschi et al., 2016).

Wallace et al. (2013) have shown that a drifting black bar promptly activates fleeing and shelter-seeking behaviour in rats, but only if shown overhead. This suggests that rats continuously monitor the space above them, to be prepared and quickly react to possible predation. The study did not investigate further what combinations of stimulus properties may be more effective to elicit rat defensive behaviour, or whether some specific kinds of stimuli would be able to elicit fleeing also when presented beside the animal, rather than overhead. Yilmaz and Meister (2013) explored some of these questions in mice. They varied the properties (e.g., luminance, contrast and speed) of a looming disc shown either overhead or below the mouse, trying to isolate the most effective stimulus parameters in evoking a defence response. Stimulation below the floor was ineffective in eliciting any behaviour. Instead, the looming black-on-grey disc reliably evoked either escape or freezing. However, the specific visual properties of the looming stimulus were critical to produce the escape behaviour − a looming white-on-grey disc, a dimming black-on-grey disc of constant size, and a shrinking (rather than enlarging) white-on-black disc were not able to trigger the defence responses. Moreover, the expansion speed of the looming object and the type of background (static or moving) also influenced the elicited behaviour, in terms of occurrence and latency. The sensitivity of mouse escape behaviour to visual stimulus properties was recently corroborated by De Franceschi et al. (2016). After confirming that a looming disc reliably elicits fleeing, the authors showed that an opposite behaviour (freezing) is evoked by a small black disc sweeping thorough the visual space above the animal. The latter behaviour was strongly influenced by the motion of the stimulus, which, at faster speeds, evoked instead the flight response. Taken together, the three studies reviewed here extend the repertoire of innate visually driven behaviours that allow investigating rodent visual cognition under very naturalistic settings, while at the same time achieving a good parametric control over key properties of the visual environment.

To conclude, it is worth mentioning a recent study investigating another kind of spontaneous, visually guided behaviour in the mouse: hunting. Hoy et al. (2016) tracked the hunting behaviour of laboratory mice engaged in prey capture of live crickets inside a square arena. By selectively restricting the access of the animals to either visual or auditory information, the authors found that mice use vision for accurate and efficient prey capture. This result was further confirmed by having the cricket placed behind a transparent acrylic barrier that reduced nonvisual cues − this manipulation did not prevent the mice to precisely target the location of the prey, despite they could not actually make contact with the cricket. Overall, this study provides another interesting example of how rodent visual abilities can be explored in a natural, yet experimentally controlled setting, although it is unclear whether further manipulations can be applied to understand what visual features (e.g., shape, colour or movement) drive prey detection, tracking and capture.

2.3 Navigation in Virtual Environments

The inspiration for developing visual tasks for rodents, based on navigation in virtual environments, comes from similar approaches, previously implemented in monkey studies (Matsumura et al., 1999; Leighty and Fragaszy, 2003; Hori et al., 2005). In the tasks that have been developed for rodents, a rat/mouse navigates a virtual visual environment, usually by running on an air-suspended spherical treadmill, in a closed loop with visual stimulation − i.e., the virtual environment is updated in real time, according to the animal movement/position, to simulate a navigation as it would happen in a physical environment. To date, most studies based on virtual reality (VR) systems have been performed on mice (Harvey et al., 2009, 2012; Dombeck et al., 2010; Youngstrom and Strowbridge, 2012; Keller et al., 2012; Chen et al., 2013; Saleem et al., 2013; Zmarz and Keller, 2016; Fiser et al., 2016), but this approach has also been applied on rats (Hölscher et al., 2005; Lee et al., 2007; Cushman et al., 2013; Aronov and Tank, 2014). This disproportion is motivated by the easier implementation of head fixation in mice and by the use of transgenic lines and viral constructs to study the neural bases underlying spatial navigation, which are more readily available in mice.

In the VR apparatus, the animal is held in place either by head fixation or body restraint − the former is more commonly applied in mice or when high stability is required to record neural activity through imaging or intracellular recordings; the latter is more typical of rat studies or when extracellular recordings with chronically implanted electrodes are performed. Both kinds of fixations imply that translational and rotational movements are not performed physically by the animal but are simulated in the virtual reality (VR) system (Thurley and Ayaz, 2016),

although some variants of the apparatus allow the body-fixed rodent to rotate on top of the ball, thus enabling physical body rotations (Hölscher et al., 2005; Aronov and Tank, 2014). Head fixation is less natural and abolishes vestibular and proprioceptive inputs during the virtual navigation but allows an easier and better control over the visual stimuli delivered to the animal — e.g., by limiting eye movements (Zoccolan et al., 2010; Wallace et al., 2013) and reducing the need to monitor and control them. Body fixation allows a more natural proprioception, but, still, it does not fully eliminate the mismatches between visual and vestibular inputs (Thurley and Ayaz, 2016).

The most common way to establish a closed loop between the animal and the visual stimulation is by using a spherical treadmill ball, which the animal is free to rotate with its paws in one or two directions, but linear treadmills and cylinders have also been used (Lee et al., 2007; Domnisoru et al., 2013). The virtual visual environment can be shown to the animal using different approaches. The simplest apparatus relies on one or more computer monitors (Youngstrom and Strowbridge, 2012; Keller et al., 2012; Chen et al., 2013; Saleem et al., 2013), while more naturalistic stimulations can be applied using panoramic toroidal or cylindrical screens, upon which the environment is projected (Hölscher et al., 2005; Lee et al., 2007; Harvey et al., 2009, 2012; Dombeck et al., 2010; Cushman et al., 2013; Aronov and Tank, 2014; Zmarz and Keller, 2016; Fiser et al., 2016). Some investigators, in an effort to make the virtual environment more natural, have also presented concurrent and appropriate stimulation in other modalities — e.g., auditory stimuli that change depending on the position of the animal (Cushman et al., 2013).

Regarding the visual tasks implemented in VR systems, only a few authors have relied on purely spontaneous navigation as a tool to investigate the neuronal basis of visual perception in rodents, without the need of any specific reward or training (Keller et al., 2012; Saleem et al., 2013; Zmarz and Keller, 2016). In most studies, the rodent subject is motivated to move along a linear virtual track by the possibility of retrieving a reward, which is delivered at the end of the track (Harvey et al., 2009; Dombeck et al., 2010; Youngstrom and Strowbridge, 2012; Chen et al., 2013; Schmidt-Hieber and Häusser, 2013; Fiser et al., 2016). Few authors have implemented a behavioural task requiring rodents to make explicit (rewarded) perceptual decisions in VR environments. Examples are tasks where an animal is trained to navigate a virtual arena and approach hidden or signalled hotspots cueing the reward location, as in a traditional Morris water maze (Hölscher et al., 2005; Cushman et al., 2013; Aronov and Tank, 2014). In other implementations, the subject is trained to choose one arm or another in a virtual T-maze, based on presentation of specific visual cues (Harvey et al., 2012). In all these experiments, a liquid reward is delivered through a licking sensor placed in front of the animal. The studies testing spontaneous exploration of VR environments are mostly concerned with understanding the neural underpinnings of spatial navigation abilities. As such, they mostly use virtual square or circular arenas, or even linear tracks. This allows a good control over the appearance of distal visual cues and enables simulating very large environments, more akin to the natural ones, where wild rodents would typically roam — something impossible to achieve with physical experimental setting. The use of a virtual arena, rather than a virtual maze, is also preferred in experiments investigating spatial learning and memory, given that the subject is free to explore the environment in every direction. Finally, the use of hidden hotspots signalling the reward location not only allows investigating memory formation of spatial cues and its effect on navigation but also makes it easer the comparison with the existing literature based on exploration of physical environments.

The linear track, which allows only 1-dimensional (1D) navigation, is probably the most used virtual setting, due to its simplicity and other factors, and its application encompasses many different kinds of investigation. First, it can be implemented with only a single monitor, and the animal movement can be either restricted in one direction on a treadmill sphere (Saleem et al., 2013; Fiser et al., 2016) or even recorded through a standard treadmill (Lee et al., 2007). This makes it easier to study the relationship between perceptual and locomotion signals, because the latter is simplified to a forward motion. The linear track also allows a better analysis of visual perception — by having visual cues of different types shown at certain segments of the track, it is possible to have a better control over the time and the way these cues are inspected by the animal, reliably linking their presentation to the underlying neural processing (Saleem et al., 2013; Fiser et al., 2016). Also, it is possible to pass from a closed loop design to an open-loop design, where the visual feedback and the concurrent locomotion behaviour are decoupled — this makes it possible to study their individual effects and interaction in visual cortex (Saleem et al., 2013; Zmarz and Keller, 2016).

As far as visual stimuli are concerned, in most VR experiments, the visual environment is made of quite simple, often parametric visual patterns — white noise patches (Saleem et al., 2013), random brick patterns (Zmarz and Keller, 2016) or sinusoidal gratings (Saleem et al., 2013; Fiser et al., 2016) are placed on the virtual walls, and it is possible to independently change their appearance or just parts of them (Zmarz and Keller, 2016). Geometrical shapes, shown in black-and-white or colours, are also used in some studies as cues to guide navigation (Youngstrom and Strowbridge, 2012; Harvey et al., 2012; Cushman et al., 2013; Aronov and Tank, 2014). In other experiments, sinusoidal or square-wave gratings are simply placed along the linear track as passive visual stimuli to probe the neuronal coding of visual information under active navigation (Saleem et al., 2013; Fiser et al., 2016). The extent to which different kinds of

visual landmarks can affect rodent navigation in virtual environments has not been extensively explored. Only one study, to our knowledge, has investigated this issue, by varying the properties of the visual cues placed along a virtual linear track (Youngstrom and Strowbridge, 2012). Specifically, the authors found that it was much easier to train mice to navigate the maze when vivid (i.e., colourful and complex) cues were posted along the walls, instead of bland ones (i.e., uniform black and grey areas). This kind of comparison needs to be further explored, for instance by directly testing rodent navigation with colour versus black-and-white stimuli, distal versus proximal cues, or landmarks placed on the lower or upper half of the animal's visual space.

Another aspect of the virtual environment that is worth discussing concerns the limitations that may disrupt the illusion of navigation. First, the virtual environment is presented over a display that is placed at a fixed distance from the observer. Thus, while motion parallax can be correctly displayed, stereo disparities are not. More importantly, it is impossible (or very hard) to simulate the physical contact with the solid elements that the animal may encounter inside the virtual environment, such as objects or walls, and prevent that the rat/mouse run across them. Some authors have tried to address this issue by having virtual objects hanging from the ceiling, so that virtual contact was impossible by design (Hölscher et al., 2005), while some others (Schmidt-Hieber and Häusser, 2013) have used air puffs as an aversive stimulation to discourage the subject from approaching the walls of the arena/track. It is also worth noticing that some investigators have developed tactile virtual environments, made of solid lateral walls that can be moved close to the animal to simulate a real corridor (Sofroniew et al., 2015), thus showing how purely visual VR systems may be potentially enriched with stimulation from other modalities to better approach the complexity of a physical environment. The question of how much a VR setting is perceived by rodents as real has been also addressed by training and testing rats and mice in equivalent physical and virtual environments (Hölscher et al., 2005; Chen et al., 2013). These studies suggest that behavioural responses and neural activity inside VR environments resemble those recorded in the physical world and call for further investigations exploring more deeply the same issue. For instance, at the behavioural level, a rodent could be trained and tested in a specific task inside either a virtual or a physical environment in interleaved sessions. Another interesting experiment would be training an animal in one kind of environment only (e.g., physical) and then testing it in the other setting (e.g., virtual) to check whether generalization is possible, or measure how long it takes for the subject to relearn the task. In all these experiments, the challenge would be making the two settings as close as possible at the perceptual level, ensuring that, in the physical environment, the visual landmarks are the only available cues to guide the animal's behaviour.

As a final remark, it is worth considering ways in which VR environments could be further explored to probe rodent perceptual and memory functions under the visual modality. One possibility is to study visual object recognition memory by implementing VR variants of the SOR tasks (see Section 2.1). The goal would be creating virtual environments resembling those used in SOR studies (i.e., an open arena, or, better, a Y-maze or a bow-tie maze) and test whether the novelty preference is still observable in such settings. If so, the VR system could then be exploited to access the neuronal substrates of recognition memory through imaging and intracellular recordings. Moreover, VR experiments would allow a better control over the properties of the visual objects − e.g., the investigator would be able to know which view of an object the rodent is perceiving, at any time during its path towards the item (especially if combined with eye-tracking), thus addressing some of the issues of SOR tasks discussed in Section 2.1.1. The same kind of approach could be exploited to probe how different appearances of visual objects are perceived by rodents and coded by the activity of their visual cortical neurons, so as to yield transformation-tolerant representations of object identity. The advantage offered by the VR system over more traditional approaches (Zoccolan, 2015; Tafazoli et al., 2017) would be the possibility to carry out such investigation under more natural viewing settings, where the pose of an object smoothly changes over the retinal image while the animal approach ad explore it. Finally, another possible application of virtual reality would be implementing in a VR setting those ethological tests of rodent innate visually driven behaviours described in Section 2.2, such as the flight-or-freeze response elicited by stimuli mimicking aerial predators. As for the case of virtual SOR tasks, the VR environment would allow a more precise control over the proprieties of the visual stimuli used to evoke the escape behaviour and would enable the access to the underlying neuronal correlates.

3. APPROACHES BASED ON EXPLICITLY TRAINING RODENTS IN VISUAL DISCRIMINATION TASKS

Studying rodent visual functions through the collection of spontaneous responses or the monitoring of innate behaviours has the main advantage of not requiring any training of the animals in cognitively demanding procedures,

such as learning the association between stimuli and correct responses. On the other hand, studies based on spontaneous behaviours have several limitations. They allow the collection of only a few trials per session; they prevent achieving a tight control over the visual properties of the stimuli; they heavily rely on the direct intervention of the investigator to keep the test going, thus potentially interfering with the animal's motivation and attention; they do not easily allow adjusting in real time the presentation of the visual stimuli to the behaviour of the animal, thus preventing the application of advanced psychophysical procedures (such as staircases or classification image methods); finally, they often do not yield objective and standardized measurements of rodent behavioural choices (e.g., exploration time, rather than number of correct choices in response to a given stimulus is recorded). These drawbacks do not prevent these methods from being extremely useful in the context of studies where vision is typically used as a mean to actually test other functions (such as the encoding and retrieval of object memories in SOR tasks). On the other hand, these limitations pose severe constraints to the study of visual perceptual abilities in rodents, i.e., to the behavioural investigation of the processing of visual information carried out by the visual systems of mice and rats. Understanding such processing requires different approaches, which involve training rodents to explicitly report their perceptual choices by learning an association between stimuli and reward. This section provides an overview of the methods that have been developed and applied to fulfil this goal.

3.1 One Stimulus − One Choice Design (Go/No-Go Task)

As anticipated in the introduction, the first step to understand a behavioural task, regardless of the experimental aim, is to analyze its design in terms of stimuli and responses. In each trial, a subject can explore or be shown a certain number of stimuli and be required to react to these stimuli by choosing among a possible set of responses. The subject's choice is collected and interpreted as a measure of the underlying perceptual or cognitive ability. According to this criterion, the simplest design in terms of structure is the one based on presentation of a single stimulus and collection of a single possible choice per trial, usually known as the *Go/No-Go task*. In this task, the subject is required to signal when he or she perceives a given stimulus feature by interacting with a sensor. The feature in question may be the presence itself of the stimulus (as in a detection task), its orientation or its motion direction. Each trial is composed by a certain number of No-Go phases, where the subject has to stand still and suspend any action, and Go phases, where he or she has to activate the sensor (and to retrieve the reward, in case of a correct choice).

This task has been applied in several studies of visual perception in rodents (Andermann et al., 2010; Histed et al., 2012; Lee et al., 2012, 2016; Glickfeld et al., 2013b; Montijn et al., 2015; Kurylo et al., 2015; Makino and Komiyama, 2015; Khastkhodaei et al., 2016) because of a few key advantages it offers over more complex tests. First, the protocol to train and test rodents in the task is relatively fast and easy − typically only a few weeks are needed to achieve a performance that is significantly larger than chance. Usually, detection accuracy and response speed are collected as behavioural measures, together with the licking or pressing pattern. Moreover, the subject's engagement can be continuously assessed by including trials with varying difficulty. For example, it is possible to monitor the motivation of the animal by using interleaved probe trials with very simple stimuli, and checking the proportion of hits, false alarms and omissions on these stimuli. Second, once the task is acquired, it is possible to gather hundreds of trials per session during the testing phase, with a performance relatively stable across several months. This is very convenient, in case neurophysiological recordings are also carried out in parallel. In fact, neuronal activity may considerably change from trial to trial, being affected by factors like task difficulty, task engagement, general arousal, stress and motivation (Gavornik and Bear, 2014; Cooke et al., 2015; Cooke and Bear, 2015; Burgess et al., 2016b). The ability to record many trials, with the animal reliably performing the same perceptual task, allows a better statistical assessment of the tuning properties of the recorded neurons in the face of such variable factors. Third, the task can be administered also to head-restrained animals − e.g., head-fixed mice or rats that have learned to stand still in a funnel (Schwarz et al., 2010; Guo et al., 2014; Kurylo et al., 2015, 2017). This makes it easier to monitor the subject's eye position and its relationship with the visual input (Stahl et al., 2000; Stahl, 2004; Zoccolan et al., 2010) and makes it possible to use the task along with neurophysiological approaches, such as two-photon imaging (Andermann et al., 2010; Montijn et al., 2015). Indeed, stillness substantially reduces any eye movements (Wallace et al., 2013) and helps obtaining enough brain stability for in vivo microscopy. In addition, the lack of locomotion makes the interpretation of neuronal responses to the visual stimuli easier (Niell and Stryker, 2010). Finally, this design does not require a complex apparatus − a monitor, a response retrieval system and a reward delivering system are sufficient.

Across studies, several different ways of collecting rodent responses in Go/No-Go visual tasks have been implemented. The most widely used approach is to monitor the licking of a touch sensor (Andermann et al., 2010; Montijn et al., 2015; Berditchevskaia et al., 2016); other methods include recording when the subject is releasing

a pressed lever (Histed et al., 2012; Glickfeld et al., 2013b), retracting from a funnel (Kurylo et al., 2015; Lee et al., 2016; Kurylo et al., 2017), or even running or not on a circular treadmill (Makino and Komiyama, 2015). The impact of choosing a method over another one has not been extensively investigated, but, at least in the case of concomitant imaging experiments, having the animal releasing a lever seems a better choice than having it licking a sensor because the latter action has been shown to induce movements in the brain (Andermann et al., 2010). With regard to the feedback provided to the animals about the outcome of their choices, in addition to deliver liquid reward in the case of correct responses, some authors penalize false alarms by either enforcing a timeout period (Montijn et al., 2015; Lee et al., 2016) or delivering an aversive stimulus, such as tail shock (Makino and Komiyama, 2015) or air puffs (Andermann et al., 2010; Berditchevskaia et al., 2016), while other investigators do not provide any feedback on incorrect choices (Histed et al., 2012; Glickfeld et al., 2013b; Kurylo et al., 2015, 2017).

The majority of the experiments employing a Go/No-Go visual task have been carried out on head-fixed mice. Fewer have been performed on rats and only under partially restrained conditions. Most studies have investigated contrast sensitivity, orientation tuning or direction selectivity, typically by presenting the rodent subjects with sine-wave or square-wave drifting gratings. For some authors, the goal was to obtain purely psychophysical measures of these visual processing abilities (Histed et al., 2012; Kurylo et al., 2015, 2017; Lee et al., 2016), while other investigators paired the behavioural tests to imaging or interventional approaches to study the underlying visual cortical processes (Lee et al., 2012; Glickfeld et al., 2013b; Montijn et al., 2015; Makino and Komiyama, 2015; Khastkhodaei et al., 2016). The task can also be easily adapted to administer stimuli under different sensory modalities. For instance, Lee et al. (2016) have tested rat ability to detect either a tactile vibration applied to the whiskers or a luminance flicker shown on a display. By varying the proportion of visual and tactile trials delivered to the animals, the authors were able to study the impact of sensory likelihood on detection accuracy and speed. The resulting sensory prioritization, due to enhanced presentation of either the visual or tactile stimuli, led to better and faster performance in test trials of the overtrained, compared to the undertrained, modality.

The simplicity in designing and implementing a Go/No-Go task does not imply that the effectiveness of the training procedure cannot be optimized by carefully monitoring and manipulating the motivational state of the rodent subject. Berditchevskaia et al. (2016) have carefully explored this possibility by testing water-deprived rats in an orientation and motion direction discrimination task. They found that both detection accuracy and motivation changed during the behavioural session, as assessed, respectively, by ROC analysis and by measuring lick frequency, efficiency, or latency. Early in the session, accuracy was reduced by the many false positives due to the overmotivated state of the animal. Once thirst started to be satiated, performance reached a stable 'optimal' regime, to eventually drop again at the end of the session, due to a decrease of the hit rate after complete satiation. These findings caution against assessing rodent accuracy in Go/No-Go tasks by averaging data collected through the entire test session. They also suggest that variations of the animal's motivational state may interact with changes applied by the investigator to stimulus conditions over the course the session, thus possibly leading to incorrect interpretations. Finally, the authors also found that well-trained rats, fully satiated before the onset of the experiment, reached better performances than those of water-deprived animals. This suggests that, while water deprivation is necessary to initially train naïve subjects, it may be later abandoned, when testing experienced animals.

Another interesting question is the relationship between the Go/No-Go task and tasks requiring more than one possible response. In a Go/No-Go task only one stimulus is paired with the reward, while the other stimuli are not. By contrast, in a multiple-alternative forced choice task (see next sections for details), each stimulus is mapped into a specific response category, which, if correctly chosen, invariably yields a reward. This means that the animal has the chance of retrieving the reward in every trial, while, in the case of the Go/No-Go task, it needs to wait before a trial comes that can possibly earn it a reward. Based on these considerations, there is a general belief that rodents may display a different level of engagement when tested in the two classes of tasks. This intuition is supported by a few studies of olfactory discrimination, showing that mice, when tested in a Go/No-Go task, spend more time to sample the stimulus, during difficult trials, in order to maintain high accuracy (Abraham et al., 2004), while mice and rats, when tested in a two-alternative forced choice task (2AFC), do not exhibit the same behaviour (Uchida and Mainen, 2003; Rinberg et al., 2006). This difference has been interpreted as the result of a speed−accuracy trade-off − in a Go/No-Go task, the preferred strategy is to have a longer sampling duration to improve accuracy per trial, while, in a 2AFC, it is to favour speed over accuracy, so as to have more trials per session and maximize, in this way, the reward rate (Friedrich, 2006; Rinberg et al., 2006). To explicitly test this hypothesis, Frederick et al. (2011) trained two groups of rats in the same olfactory discrimination task, using either a Go/No-Go or a 2AFC, but they found a substantial equivalence between the two designs, in terms of general performance and stimulus sampling duration. A comparison between the two tasks in the study of visual perception was recently carried out by Long et al. (2015), who investigated discrimination of oriented gratings in mice engaged in either a 2AFC or a Go/No-Go task.

The authors administered sessions with gratings presented either at full contrast only or spanning a range of contrasts. They found that full-contrast stimuli were better discriminated in the former sessions, regardless of task design. However, mice tested in the 2AFC task with multiple contrasts showed better performance at high-contrast levels, compared to mice tested in the Go/No-Go task. The lower performance in the latter case was explained by an increase in response bias, likely due to a reduction of the animal's internal threshold to respond, as it adapted its perceptual strategy to deal with a range of stimulus saliencies. This suggests that 2AFC tasks are better suited than Go/No-Go tasks to assess the influence of parametric changes of stimulus properties on rodent discrimination accuracy because they are more robust to variation of the animal's response criterion.

3.2 Two Stimuli − Two Choices Design (2-Stim/2-Choices)

Since the pioneering experiments of rat visual perception carried out by Lashley and his contemporaries (Lashley, 1930a,b, 1938; Munn, 1930; Fields, 1932, 1935; 1936; Krechevsky, 1938a,b), the most widely used behavioural task to study rodent visual functions has been the paradigm known as *spatial two-alternative forced choice task*, or, more simply, *two-alternative forced choice task* (2AFC) or even *two-alternative choice task*. As the name indicates, the task involves the rodent subject choosing between two possible alternative stimulus categories. The choice is forced, in the sense that the task does not contemplate the possibility for the animal to explicitly report a possible inability to decide between the two stimulus categories, although the rat/mouse can choose not to respond to a given stimulus, thus ignoring the trial. Per se, the name does not indicate whether one stimulus at the time is presented to the animal (as in the Go/No-Go task), or, instead, two stimuli are simultaneously shown in each trial. However, most authors implicitly assume the latter kind of design − i.e., with the rodent subject required, in every trial, to compare two visual stimuli and choose the one belonging to the perceptual category associated to a positive reinforcement (e.g., reward), usually referred to as S+ (while S− is used to denote the stimulus yielding no reward and/or a negative reinforcement). It is our opinion that assuming the simultaneous presentation of two stimuli, when referring to a 2AFC task, is misleading, since also tasks based on presentation of a single stimulus per trial, but still requiring the animal to choose between two response categories, fit, semantically, this definition − as a matter of fact, such designs are often referred to as *two-alternative choice tasks* (Carandini and Churchland, 2013). Because of this, in the following, we use the definition *two-alternative forced choice* (and its acronym 2AFC) to indicate, collectively, both kinds of tasks, while adopting the acronyms 2-Stim/2-Choices and 1-Stim/2-Choices to specify whether, respectively, two stimuli, or only one, are shown per trial. This section will provide a critical overview of experiments based on 2-Stim/2-Choices tasks, while the next section will present and discuss 1-Stim/2-Choices tasks.

One of the earlier and most successful implementations of 2-Stim/2-Choices tasks to probe rodent vision was Lashley's jumping stand apparatus (Lashley, 1930a,b, 1938). This system required a rat to jump towards a target S+ stimulus card from a distance of 20 cm, while avoiding a flanking S− stimulus card. The S− card was rigidly fixed to a wooden wall, thus causing the animal to bang into it, in case of an incorrect choice, and fall into a net underneath the apparatus. Instead, the S+ card was held in place by a light spring, so that, when the rat jumped against it, the card fell back and the animal was able to reach a landing platform with reward (solid food). Using this apparatus, Lashley successfully tested pigmented rats in a variety of visual discriminations. Most noticeably, he was able to provide the first account of processing of shape information in a rodent species, by training rats to discriminate simple geometrical forms, such as a triangle versus a circle or an upward versus an inverted triangle. In addition, Lashley found that rats were capable of generalizing the discrimination to slightly transformed appearances of the previously learnt shapes (e.g., size and luminance changes), thus pioneering the study of invariant object recognition in this species (Zoccolan, 2015). The jumping stand apparatus became a popular tool to investigate rat pattern vision, successfully used by several of Lashley's contemporaries. Most noticeably, Krechevsky applied the jumping stand to show that rats are capable of perceptual grouping − i.e., of perceiving arrays of dots, differentially aligned along the vertical and horizontal dimensions, as oriented patterns (Lashley, 1930a,b). Later investigators (Sutherland, 1961; Sutherland and Carr, 1962; Sutherland et al., 1962; Sutherland and Williams, 1969) simplified this design, by implementing the 2-Stim/2-Choices task in a rectangular operant box, with a starting area and a discrimination area, located on opposite walls of the box. On the wall of the discrimination area, the investigator placed two shapes cut out of white Perspex, with a drinking nozzle (for delivering liquid reward) protruding through the middle of each shape. Rats were trained to leave the starting area and approach a fixed S+ pattern (while ignoring the other S− stimulus) to collect the reward.

The main drawback of these early designs was that, similar to the behavioural rigs used in standard SOR tasks (see Section 2), they required the manual intervention of the investigator to relocate the rat on the starting platform or area, before each new trial. This strongly limited the number of trials that could be collected per session and,

therefore, the number of stimulus conditions that could be tested per experiment and the statistical power to evaluate rat discrimination accuracy. Another weakness of this approach was the use of cardboard visual stimuli or physical 2D patterns (due to the obvious technical limitations of the time), which also contributed to constrain the number of possible stimulus variations tested by the investigator across trials. Finally, only static stimuli could be shown. Some of these limitations have been addressed by more recent variants of the 2-Stim/2-Choices task, which exploit the possibility to show visual stimuli over computer controlled stimulus displays.

A widely used implementation of the 2-Stim/2-Choices task was developed by Prusky et al. (2000), which combined a Morris water maze (Morris, 1981; Sutherland and Dyck, 1984) with a 2AFC design. The result was a Y-maze pool, with a starting area located at the base of the Y, and two computer monitors placed at the end of the two arms stemming from the bifurcation. A hidden platform was placed underwater, in front of just one of the monitors, i.e., directly under one of the visual stimuli. The animal had to reach the monitor showing the S+ stimulus to escape the water and be allowed to rest for a few seconds on the platform. In their first study, Prusky et al. used this apparatus to train mice and rats to discriminate between a sine-wave grating and a grey screen, thus assessing contrast sensitivity in both species in just a few trials and sessions. In fact, the main advantage of this design is the relative ease to train the animals because the aversive motivation of water-induced stress is very powerful in driving the rats and mice to learn. Among the drawbacks, there is the fact that the intervention of the investigator is still required to move back and forth the subjects from the hidden platform to the starting area, and this, together with the fatigue this task imposes on the animal, implies that only a limited number of trials (20−40) can be collected per session. Another concern is the impossibility to precisely know the distance at which the subjects make their choice, when they swim along the starting arm of the Y maze, since the location of the bifurcation only imposes a lower bound to such distance. This implies that the size of the visual stimuli is not fully controlled, and, as a consequence, the perceptual ability under investigation (e.g., contrast sensitivity) is measured with a limited precision. Finally, the system, due to the presence of freely moving animals in a liquid medium, can hardly allow concomitant neurophysiological recordings. In spite of such limitations, following its introduction in 2000, the Prusky's water maze has been employed to investigate many different aspects of visual processing in rodents: visual acuity and contrast sensitivity (Prusky et al., 2000, 2002, Prusky and Douglas, 2003, 2004); memorization and recognition of 2D, high-contrast images (Prusky et al., 2004b; Driscoll et al., 2005; Davies et al., 2007; Vermaercke et al., 2015); motion discrimination (Douglas et al., 2006); categorization of natural and artificial movies (Vinken et al., 2014) and category learning (Vermaercke et al., 2014a).

Another approach to implement a 2-Stim/2-Choices task in a Y-maze had been previously introduced by Gaffan et al. (Gaffan and Eacott, 1995; Gaffan and Woolmore, 1996), who applied and further developed it in a series of later studies (Simpson and Gaffan, 1999; Gaffan et al., 2000, 2001, 2004; Eacott et al., 2001, 2003). The apparatus consisted of a Y-maze, with three identical arms (i.e., same length and same angle between each pair of arms) and a pair of computer monitors located at the end of each arm (for a total of six stimulus displays), where the reward was also administered, through a food pellet delivery system. Visual scenes of various complexities were displayed on the monitors, with the scenes shown in the adjacent monitors being the mirror version of each other along the vertical axis. The motivation behind the presentation of such paired visual scenes was to show to the rats the same visual stimulus, regardless of the arm from which it would inspect the monitors. In fact, in this design, the arm where the animal made its perceptual discrimination in a given trial became the starting arm for the next trial. To train the rats, the authors used either a constant-positive or a constant-negative paradigm, in which two different scenes were displayed at the end of the two arms not currently occupied by the animal. One of these scenes remained fixed (constant) across trials, while the other changed on a trial-by-trial basis. The rat had to learn to always approach (S+) or always avoid (S−) the constant scene. The strength of this design rested precisely on the possibility to change the variable scene along a variety of stimulus dimensions (e.g., number, size, shape, colour, contrast and luminance of the objects each scene contained), so as to assess its perceived similarity to the constant scene. Thanks to this design, Simpson and Gaffan (1999) were the first to provide solid evidence about rat ability to process visual objects/scenes by extracting and processing shape information, as confirmed by more recent investigations (Zoccolan, 2015). Also important, in Gaffan's design, was the possibility to have the animal performing the task across a continuous sequence of trials, without the need of human intervention, thus increasing the number of trials per session. Yet, Gaffan's apparatus was still affected by the same limitation of other implementations of the 2-Stim/2-Choices task, such as Prusky's water maze − it did not allow determining the viewing distance and position of the stimuli, thus affording only a limited control over the retinal size and position of the visual objects.

Other recent implementations of the 2-Stim/2-Choices task that, differently from Prusky's water maze, have the advantage of not requiring handling the animals during the experimental session are based on the use of a small

operant box, equipped with a monitor, response sensors and one or more reward-delivery systems. These systems are simpler, compared to Gaffan's apparatus, since they have a single stimulus display, where the two visual stimuli are shown side by side, and the movement of the animal, although not fully prevented, is reduced by the small size of the box (typically a few tens of cm per side) (Bussey et al., 1994). The location of the stimuli is always spatially matched to the location of the response sensors, but the specific way of collecting the responses varies across studies. The animals can respond to the stimuli: (1) by placing their nose in one of the several nose pokes, each equipped with a infrared beam, or directly licking some touch sensors (Meier et al., 2011; Clark et al., 2011; Vermaercke and Op de Beeck, 2012; Meier and Reinagel, 2013; Petruno et al., 2013; Long et al., 2015); (2) by pressing one of two levers (Cook et al., 2004; Carlsson and Swedberg, 2010) or (3) by directly touching an infrared or a pressure-sensitive touchscreen (Bussey et al., 1997, 2008; Cook et al., 2004; Minini and Jeffery, 2006; Romberg et al., 2013; Horner et al., 2013; Oomen et al., 2013; De Keyser et al., 2015; Bossens et al., 2016; Stirman et al., 2016). The reward for a correct choice can be a food pellet, delivered through a dispenser, located on the other side of the operant box (Bussey et al., 1997; Minini and Jeffery, 2006; Carlsson and Swedberg, 2010; De Keyser et al., 2015) or a liquid (such as water or milk), delivered through a cannula inserted in the nose poke (Meier et al., 2011; Long et al., 2015) or directly through the touch sensor (Vermaercke and Op de Beeck, 2012; Petruno et al., 2013; Burgess et al., 2016a; Stirman et al., 2016) or even in a single, separate location (Cook et al., 2004).

The way in which rodent choices are collected must be selected carefully since it may influence the speed of training, as well as the yield of the experiment and the animals' performance. For instance, Cook et al. (2004) found that the rate of learning was faster when the rats were trained to respond to the stimuli by directly touching them on the touchscreen, rather than by pressing a lever, although discrimination accuracy was not altered. Also the choice of the screen may matter — Bussey et al. (2008) observed that delivering an answer on an infrared, instead of a pressure-sensitive screen was easier for the rats, and affected their performance.

The visual stimuli tested in such single-screen operant boxes varied considerably across studies, depending on the visual function being investigated. Most studies have used simple high-contrast shapes (Bussey et al., 1997; Cook et al., 2004; Minini and Jeffery, 2006; Vermaercke and Op de Beeck, 2012; De Keyser et al., 2015), while other authors have tested oriented gratings (Carlsson and Swedberg, 2010; Meier et al., 2011; Long et al., 2015; Burgess et al., 2016a) or random fields of drifting dots (Stirman et al., 2016). The high yield of trials afforded by these systems (in the order of a few hundreds per session), along with the possibility of manipulating the visual stimuli on a trial-by-trial basis, has allowed exploring visual perceptual and memory functions in a more refined and systematic way, compared to other implementations of the 2-Stim/2-Choices task (e.g., Prusky's water maze). For instance, Clark et al. (2011) tested rat ability to discriminate pairs of morphed objects with various degrees of similarity, while also occluding specific quadrants of the stimulus display, so as to check whether the animals processed the entirety of the stimuli. De Keyser et al. (2015) trained rats to discriminate two orthogonally oriented bars, initially shown at high contrast, as white stimuli against a black background. They then altered the visual cues that defined the bars, finding that the rats were still capable of extracting the shape of the stimuli, even when the latter were defined only by second-order cues (i.e., texture differences between figure and ground). As a further example, Vermaercke and Op de Beeck (2012) applied a classification image approach to randomly occlude, on a trial-by-trial basis, the geometrical shapes that a group of rats had been trained to discriminate, thus investigating the perceptual strategy underlying rat perceptual decisions (see Section 4.2 for details). All these applications of the 2-Stim/2-Choices task in the single-screen operant box nicely show how this method allows studying the perceptual mechanisms deployed by rodents to process visual information. However, one important limitation of these experiments rests in the nature itself of the task, i.e., the simultaneous presentation of two stimuli, which makes it hard to apply independent manipulations to each stimulus separately — this issue is discussed at length in the next section, when comparing 2-Stim/2-Choices to 1-Stim/2-Choices tasks (see also Section 4.2).

As a final remark, it is worth pointing to a few methodological studies that made an inventory of all the potential experimental procedures that can be implemented using touchscreen-based operant boxes in order to investigate visual cognition using rodent models (Horner et al., 2013; Mar et al., 2013; Oomen et al., 2013). It is also interesting to mention some of the authors that tried to push the boundaries of the 2-Stim/2-Choices design, by allowing presentation of more than two stimuli at the same time and collection of more then two responses from the rodent subjects (Keller et al., 2000; Bari et al., 2008; Botly and De Rosa, 2012; Mar et al., 2013). One possible implementation is the 5-choice serial reaction time task, which makes it possible the assessment of visual attentional processes in rodents (Bari et al., 2008). Other authors have measured contrast sensitivity in rats tested with a 6-alternative choice task (Keller et al., 2000), while still other investigators have studied the visual search of specific features in simple 2D shapes with a 4-,6- or even 8-alternative choice task (Botly and De Rosa, 2012), thanks to the use of

touchscreen technology. These variants of the alternative choices task, however, are still rarely used, likely not only due to the difficulty, for the animals, to deal with multiple sources of visual information and multiple spatial locations, but also because of the complexity of the experimental rigs.

3.3 One Stimulus – Two Choices Design (1-Stim/2-Choices)

A more advanced experimental design to probe rodent visual functions is based on the presentation of a single stimulus per trial (as in the Go/No-Go task), but with the collection of two possible alternative responses from the animal. Hence, the name of this paradigm, often called *two-alternative choice* task (see discussion in the previous section), although we will refer to it with the acronym *1-Stim/2-Choice*s, to distinguish it from other variants of the two-alternative choice task, such as those involving the simultaneous presentation of two visual stimuli (see Section 3.2). The main difference with the Go/No-Go task is that the subject is required to make and report a decision on every trial, sensing the stimulus and choosing between two possible response categories (i.e., object identities or pattern orientations). As mentioned in the previous section, this endows the animal with the possibility to gain a reward in every trial, without the need of waiting for the occurrence of a Go stimulus. As previously discussed, this can potentially make the motivation of the animal to respond correctly in each trial lower, as compared to a Go/No-Go task. On the other hand, the need for the animal to decide between two possible choices makes it easier to understand which responses represent true decisions and also makes the task more solid to fluctuation of the subject's motivational state during the session. In fact, the variation of response rate produced by such fluctuations will equally affect both choices, without altering the proportion of hit and false alarms (in a 2AFC task, correct and incorrect choices can be considered as, respectively, hits and false alarms; see Carandini and Churchland, 2013.

With regard to the apparatus used to implement the 1-Stim/2-Choices task, the main difference among the rigs described in the literature concerns the freedom given to the animal in terms of positioning during the task. The subject can be (1) free to move its body, while sensing the stimulus, interacting with the sensors used to retrieve its responses, and collecting the reward (Bussey et al., 1997; Meier et al., 2011; Busse et al., 2011; Raposo et al., 2012; Gleiss and Kayser, 2012; Meier and Reinagel, 2013; Reinagel, 2013; Petruno et al., 2013; Siemann et al., 2015); (2) head-fixed (Scott et al., 2015; Burgess et al., 2016a) or (3) partially restrained, with its body still and the head making small movements to interact with the sensors and collect the reward from apposite ports (Kurylo et al., 1997; Sakata et al., 2004; Hirokawa et al., 2008; Kurylo, 2008; Kurylo and Gazes, 2008; Zoccolan et al., 2009; Tafazoli et al., 2012; Alemi-Neissi et al., 2013; Rosselli et al., 2015). For instance, partial body/head restraint can be achieved by requiring the animal to insert its head into a viewing hole (3–4 cm in diameter) that faces the stimulus display and gives access to the response/reward ports – e.g., see Zoccolan et al. (2009). This arrangement forces the head of the rodent to remain remarkably stable during the first ~500 ms following stimulus presentation (Alemi-Neissi et al., 2013), which, in turn, allows a precise control over some important features of the stimulus, such as size, but also position and orientation, if eye movements are assumed to be absent or very sporadic, as typical of head-fixed rodents (Zoccolan et al., 2010; Wallace et al., 2013). Alternatively, a transparent glass funnel can be used, where the rodent learns to insert its head and stay still during stimulus presentation, and only later move to the response/reward locations – e.g., see Kurylo et al. (1997).

The visual stimuli are typically presented over a computer monitor placed in front of the animal or are delivered through discrete light sources (e.g., LEDs), in case of simple light detection tasks. Responses are retrieved either through licking (touch) sensors or nose pokes, where the rodent is trained to insert its snout. In most implementations, the task is self-paced by the animal, which actively triggers stimulus presentation by means of an apposite sensor placed in front of the stimulus display (Sakata et al., 2004; Hirokawa et al., 2008; Zoccolan et al., 2009; Tafazoli et al., 2012; Raposo et al., 2012; Gleiss and Kayser, 2012). This likely contributes to keep the attention of the animal focused on the stimulus discrimination and its engagement in the task high throughout the testing procedure (Marbach and Zador, 2017).

Reward is typically liquid and is usually delivered at the same locations where the responses are retrieved, using feeding needles that either work as response sensors or are placed inside the nose pokes. Only in a few studies, the reward for both choices was provided in a single location (as a solid food pellet), different from the positions of the response sensors (Bussey et al., 1997; Sakata et al., 2004; Hirokawa et al., 2008). The relative advantages of these two kinds of reward delivery have not been empirically tested, but it is reasonable to assume that providing the reward at the response locations makes it easier for the animal to learn the correct associations between stimuli and responses. Moreover, such procedure substantially increases the speed of execution of the task because the subject does not waste time to move its head/body to a different location after making the response – typically, several hundreds of trials per session can be collected in 1-Stim/2-Choices tasks where the reward and response locations are identical

(Zoccolan et al., 2009). On the other hand, if this reward delivery system is implemented, special care must be taken to ensure that both reward ports always work equally well during the task and deliver the same amount of liquid. Otherwise, the animal may develop a bias towards the port yielding more reward, altering the proportion of hits and false alarms to the two stimuli.

1-Stim/2-Choices tasks have been applied to investigate a range of visual processes, using stimuli of various complexities, presented either in front or to the side of the rodent subject. At the more basic level, some experiments have employed visual stimuli as simple as flashes of light. These could appear at either side of the animal, alone or paired with another sensory stimulus, to measure detection thresholds across different modalities (Sakata et al., 2004; Hirokawa et al., 2008; Gleiss and Kayser, 2012; Siemann et al., 2015). In other studies, trains of flashes with different frequencies were presented, with each frequency linked to a different response location (e.g., low rate: go to left; high rate: go to right) to study rate discrimination or evidence accumulation (Raposo et al., 2012; Sheppard et al., 2013; Odoemene et al., 2017). These experiments are simple in their design since they require manipulating only two basic stimulus parameters — intensity and frequency of the light pulse trains. As such, this design is ideal to deliver, alternatively to or concomitantly with the visual stimulation, sensory stimuli of other modalities (e.g., auditory or tactile), varied along the same parametric axes (Sakata et al., 2004; Hirokawa et al., 2008; Raposo et al., 2012; Gleiss and Kayser, 2012; Sheppard et al., 2013; Siemann et al., 2015; Odoemene et al., 2017). This allows manipulating the amount and type of information delivered, independently, through each sensory channel, thus creating a variety of interesting stimulus combinations. For instance, one modality can be made more salient than the other, or the stimuli delivered to one sense can be made coherent or in conflict with those delivered to another sense, so as to dissect the mechanisms underlying the enhancement of perceptual acuity under multimodal sensing (Raposo et al., 2012, 2014; Gleiss and Kayser, 2012; Sheppard et al., 2013).

While very powerful to investigate basic principles of cross-modal perception or multisensory integration, the use of simple light pulses offers little insight into higher-order processing of visual information. Much richer and structurally more complex visual stimuli have been deployed to understand shape processing, object recognition and motion perception in rodents: 2D black-and-white shapes (Bussey et al., 1997); oriented gratings (Meier et al., 2011; Meier and Reinagel, 2013); static arrays of dots (Kurylo et al., 1997; Kurylo, 2008; Kurylo and Gazes, 2008); random fields of drifting dots, with variable degrees of coherent motion (Meier and Reinagel, 2013; Petruno et al., 2013); and 2D renderings of 3D objects, made of multiple structural elements (Zoccolan et al., 2009; Tafazoli et al., 2012; Alemi-Neissi et al., 2013; Rosselli et al., 2015). Describing such a variety of studies is beyond the scope of this chapter, whose goal is to provide a critical overview of methodological approaches rather than a discussion of scientific findings about rodent vision — for a review of the latter, see Zoccolan (2015). However, it is worthwhile to look deeper into some of these studies to emphasize the distinguishing features of the 1-Stim/2-Choices task, as compared to other approaches, also widely applied to investigate rodent visual perception, such as the 2-Stim/2-Choices tasks described in the previous section. In these tasks, two stimuli are simultaneously presented to the subject. This facilitates the acquisition of the task since the animal can simply learn to approach the positively reinforced stimulus, with no need to learn and memorize an association between stimulus category and reward location (see previous section). On the other hand, the simultaneous presence of both discriminanda on the stimulus display allows the stimuli to be more easily distinguished on the base of low-level, accidental visual properties, rather than higher-order shape information. The 1-Stim/2-Choices task, where only one stimulus at the time is shown to the subject, can effectively prevent this issue, when the stimulus set is properly designed.

As an example, it is worth considering the tests of rat visual object recognition carried out by Zoccolan and colleagues, using a 1-Stim/2-Choices task (Zoccolan et al., 2009; Alemi-Neissi et al., 2013; Rosselli et al., 2015). In these studies, the animals were first trained to discriminate the default views of two visual objects. They were then presented with many different transformed views of the same two objects, obtained by varying their position, size, orientation, lighting, etc. The animals were thus tested for their ability to correctly identify the objects in spite of these changes in their appearance, thus assessing rat proficiency to perform invariant object recognition (see Introduction). The use of the 1-Stim/2-Choices task was critical to successfully perform this assessment. In fact, the two objects, when considered in a given pose, could contain some low-level features allowing the rats to trivially distinguish them — examples are possible differences of overall luminosity, contrast, area, etc. Such differences would be preserved if the objects were equally transformed (e.g., equally scaled or translated) and then shown side by side to the rats, as in 2-Stim/2-Choices tasks — e.g., see Minini and Jeffery (2006) and Vermaercke and Op de Beeck (2012). By contrast, in the 1-Stim/2-Choices task implemented by Zoccolan et al. (2009), each object view was shown in isolation, thus forcing the animals to implicitly compare the current view with every possible appearance of both objects the rats may have previously experienced. This eliminated possible low-level, transformation-invariant cues, such as luminance differences, and forced the animals to deploy a truly advanced, transformation-tolerant

processing strategy. It was likely thanks to this design that the authors found a level of invariant recognition (Zoccolan et al., 2009) and a complexity of shape processing strategy (Alemi-Neissi et al., 2013; Rosselli et al., 2015) that was superior to that reported by some previous and later studies based on 2-Stim/2-Choices tasks (Minini and Jeffery, 2006; Vermaercke and Op de Beeck, 2012). More in general, the single stimulus presentation allows applying stimulus and task manipulations that are necessary to implement advanced psychophysical procedures. Examples are the visual priming paradigm (Tafazoli et al., 2012) and the classification image approaches (Alemi-Neissi et al., 2013; Rosselli et al., 2015) described in Section 4, which would otherwise be impossible (visual priming) or less well controlled (classification image) if multiple visual patterns were shown on the stimulus display (Vermaercke and Op de Beeck, 2012).

An aspect of 1-Stim/2-Choices tasks that is worth discussing is how the rodents are habituated to the experimental rig and initially shaped in the visual discrimination, before being tested in the final version of the task. Shaping procedures vary considerably across studies and are often not described in details, but they typically involve initially presenting the animals with stimuli that are easier to discriminate, compared to the stimuli shown during the testing phase. For instance, in an experiment requiring the discrimination of two visual shapes, one of the two items can initially be presented at very low contrast, to help the rodent acquiring the discrimination based on very salient differences in terms of global, low-level features. As an alternative, each shape can be initially paired to a specific sound cue, which is easier to parse and classify, compared to a complex visual pattern. Both procedures can be very effective in the initial shaping of the animals (Zoccolan; personal communication) but have an important drawback. In both cases, the subject is initially induced to solve the task by relying on differences along perceptual dimensions (or modalities) that are not those the investigator intends to test in the final version of the experiment. This causes two potential problems. First, it can take a lot of time and effort for the animal to eventually unlearn the original discrimination (i.e., to unlearn relying on contrast differences or sound cues) — a slow and gradual reduction of the differences along the stimulus dimensions used during the shaping phase is typically necessary. More importantly, there is a risk that the subject will continue to partially rely on such differences, whenever available, to discriminate the stimuli in the test phase. This requires to carefully match the test stimuli in terms of the low-level features used during shaping (e.g., contrast or luminance) or to introduce large enough variations of these features across the stimulus set, so as to make them fully ineffective as cues of stimulus identity.

Another aspect of the training and testing procedures that must be carefully monitored in 1-Stim/2-Choices tasks is the tendency of rodents to develop stereotypical response habits, such as the bias towards one of the response/reward locations or a response alternation strategy. During shaping and training, the emergence of these habits can be detected by monitoring in real-time the proportion of choices of the left and right response ports. This allows counteracting such unwanted (because stimulus unrelated) behaviours by (1) altering the proportion of trials requiring a left and right response; (2) decreasing the amount of reward delivered at the biased reward location; or (3) repeating the presentation of failed trials until the animal makes a correct response. Obviously, such interventions need to be abandoned at the end of the shaping/training phase, before the actual experimental test phase takes place. One precaution that can instead be adopted during the whole experiment is to use a pseudorandom stimulus presentation protocol, where the maximal number of consecutive stimuli that require choosing the same response location is constrained to be 3 or 4. This helps preventing the development of bias habits, due to the occasional, more frequent presentation of stimuli belonging to the same response category. That rodent perceptual decisions can be affected by the sequence of previous correct and incorrect choices has been empirically shown by two recent studies (Scott et al., 2015; Odoemene et al., 2017). Rats and mice, in fact, display a win-stay-lose-switch approach to decision-making, confirming rewarded choices and abandoning unrewarded ones, regardless of stimulus identity/features. This bias builds up incrementally, when multiple consecutive trials earn the animal a reward from the same location, but even a single choice can influence the animal's decision up to three trials in the future. When detection or discrimination measures are collected along a parametric stimulus axis, this bias can be detected as a shift of the resulting psychometric curve (Carandini and Churchland, 2013).

Most studies employing the 1-Stim/2-Choices task have been performed on freely moving or only partially restrained rats, as rats are better subjects than mice for experiments investigating advanced decision-making or perceptual abilities, while head fixation is a procedure more commonly applied to mice (given their lower weight and strength). Two notable exceptions are the studies of Burgess et al. (2016a) and Scott et al. (2015), where, respectively, head-fixed mice and head-fixed rats were tested in a complex 1-Stim/2-Choices task. It is worth reviewing these studies since they illustrate interesting developments of the task from a methodological standpoint.

In Burgess et al. (2016a), a head-fixed mouse was shown drifting oriented gratings at various contrasts, presented either to its left or right side over a stimulus display. The animal had to report detection of the stimulus by turning a steering wheel, so as to bring the grating at the centre of the display, which earned it a reward. The innovative feature of this experimental protocol is the closed loop between the actions of the mouse and the visual stimulus.

The authors exploit it to collect large amounts of contrast sensitivity data following rapid learning (a few weeks) of the task, thanks to the intuitive coupling between stimulus location and steering direction. However, one could devise more powerful and intriguing applications of the method to investigate, for instance, invariant visual object recognition. A mouse (or a rat) could be first trained to discriminate the default views of two visual objects, as in Zoccolan et al. (2009). The animal could then be trained to virtually manipulate, by means of a wheel or a trackball, transformed (e.g., shifted or in-depth rotated) views of the objects, so as to bring them to match the previously leaner default views. The accuracy, latency and speed of the choices might be used to assess how similar each transformed view is perceived to the default one. If paired with neuronal recordings, this procedure would also allow to insert unexpected views along the smooth flow of transformations produced by the steering of the wheel/ball, so as to investigate the neuronal correlates of novelty detection in visual cortex (Vinken et al., 2017), during an active (although virtual) object manipulation. It should be emphasized that it is the virtual manipulation of the visual stimulus that sets this study apart from previous applications of closed loop designs, where it is the animal's locomotion to be linked to a virtual visual environment (Saleem et al., 2013; Zmarz and Keller, 2016) − with the latter approach enabling a much rougher control over the properties of the visual input (see Section 2.3).

With regard to the study of Scott et al. (2015), the authors were able to measure the accumulation of perceptual evidence in rats presented with light flashes, either to their left or right side. The task of the animals was to indicate the side where the larger number of flashes was shown. The main novelty of this experimental design was that it paired a complex visual perceptual task with the voluntarily head-restraint that the authors had developed in a previous study (Scott et al., 2013) − rats were successfully trained to insert their head into a head-port, where a previously implanted head-plate was automatically held in place for up to 7 s by pneumatic pistons. After stimulus presentation they were left free to approach apposite nose pokes to deliver their response. The rationale is that voluntary head-restraint is supposed to be less stressful, as compared to forced restraint, thus facilitating behavioural testing (Scott et al., 2013). The obvious advantage is the reduction of head movements, which allows the use of in vivo cellular resolution imaging and perturbation techniques.

4. ADVANCED PSYCHOPHYSICAL PROCEDURES

In the previous sections, we have provided an overview of the behavioural methods to study visual perception in rodents, at the level of both apparatus and basic experimental design. Here we illustrate how these methods can be applied to probe rodent visual functions by implementing psychophysical procedures as advanced as those used in primate studies.

4.1 Configural Visual Discrimination Tasks

In this class of tasks, a subject needs to learn discriminations of composite visual patterns that require the concurrent processing of multiple visual features. By design, none of the patterns can be distinguished from the others by relying on a single constituent element because each element appears equally likely in all the stimuli. These tasks are powerful psychophysical tools because they allow assessing whether an observer is able to process complex visual objects by relying on a configural strategy, as opposed to a featural one − i.e., by processing not only the properties (e.g., the shape) of individual features but also their relations (i.e., their co-occurrence in specific spatial relations). In humans, a typical example of configural processing is the recognition of faces and other multifeatural complex objects, such as greebles (Maurer et al., 2002). In monkeys, configural tasks have been used to assess the impact of learning on the tuning for complex visual objects of higher-order visual cortical neurons (Baker et al., 2002; Cox and DiCarlo, 2008). In rodents, these tasks have been mainly applied to investigate the involvement of hippocampus and parahippocampal cortices in learning complex pattern discriminations (Eacott et al., 2001; Driscoll et al., 2005; Davies et al., 2007).

The most common variant of configural tasks is biconditional discrimination, where four different visual elements (i.e., A, B, C and D) are combined to obtain four different compound patterns (i.e., AB, AC, DB and CD). The patterns can be divided into two sets, each containing two stimuli that do not share any elemental feature − i.e., patterns AB and CD (set #1) versus patterns AC and DB (set #2). By requiring a subject to associate to opposite response categories these two sets (i.e., with set #1 only being rewarded), a configural discrimination is enforced since each pattern can be distinguished from the others only by concurrently considering both its constituent elements. Since it is relatively easy to train monkeys in tasks requiring more than two forced choices (e.g., by instructing the animal to saccade to multiple response locations over the stimulus display), in primate studies a single compound stimulus

can be presented in each trial, with the animal reporting its identity among the four possible choices (Baker et al., 2002; Cox and DiCarlo, 2008). In the case of rodents, since tasks involving more than two choices are possible but impractical (see Section 3.2), biconditional discrimination has been implemented in the form of multiple two-alternative forced-choice tasks (i.e., AB+ vs. AC−, CD+ vs. DB−, AB+ vs. DB− and CD+ vs. AC−, where the + and − symbols denote the two response categories), administered to the animals in interleaved trials or small blocks of trials (Eacott et al., 2001; Davies et al., 2007; Bossens et al., 2016).

Among the three studies that have employed this paradigm, two found that rats are capable of biconditional discrimination (Eacott et al., 2001; Davies et al., 2007), while the third one failed to find any evidence that rats can learn such as highly nonlinear perceptual task (Bossens et al., 2016). Such conflicting findings can possibly be explained by the different designs used to produce the compound patterns in the three studies. Eacott et al. (2001) did so by superimposing the constituent elements of the patterns on top of each other. This procedure created unique features at the intersections of the elements, thus possibly allowing the animals to succeed in the task using a featural, rather than a configural, strategy. A stricter configural task was implemented by Davies et al. (2007), who created the compound stimuli by juxtaposing two rectangular elements, each bearing a specific, black-and-white visual shape. Yet, rats successfully learned this task, achieving higher than chance performances correct in just about 12 training sessions. Such a capability to concurrently process truly configural stimuli is consistent with an earlier report by Driscoll et al. (2005), who relied on similar high-contrast patterns but used a different variant of configural discrimination, known as transverse patterning (for a brief description of the task see Zoccolan, 2015). The study in which rats did not acquire the biconditional discrimination (Bossens et al., 2016) was based instead on compound patterns made of a common vertical bar plus two shorter horizontal bars, placed on each side of the central common element, but at a variable, pattern-specific height (e.g., one category of stimuli contained the crosslike pattern † and its 180°, in-plane rotated version). Because of such stimulus design, the constituent elements of the compound patterns (i.e., the short horizontal bars) differed not in terms of their shape, as in the previous studies (Davies et al., 2007; Bossens et al., 2016), but in terms of their position along the central, vertical body. This suggests that rat ability to succeed in such complex, configural discriminations depends on the specific visual property (i.e., shape or position) being manipulated to create the compound patterns. As such, these findings call for further investigations, exploring additional stimulus dimensions and possibly paired with neurophysiological recordings, so as to fully exploit the potential of this class of behavioural tests in the assessment of high-level visual processing in rodents.

4.2 Classification Image Approaches

Behavioural assays yielding accuracy measurements are useful insofar as they reveal the limits and capabilities of visual perception of a given species, when tested in a specific visual detection or discrimination task (e.g., orientation discrimination or invariant object recognition; see Section 3). Such measurements, however, dot not typically allow inferring the perceptual strategies underlying the visual abilities under investigations. In other words, accuracy measurements can tell whether and the extent to which an observer is proficient in a given visual task, but they cannot tell why the observer is able to succeed in the task − i.e., what perceptual mechanisms the subject deploys to process the visual input and successfully extract task-relevant information.

A class of different approaches, known as *classification image* methods (Murray, 2011), can be applied to achieve this kind of understanding. These methods consist in applying additive or multiplicative noise to the visual stimuli a subject has previously learned to recognize, so as to obtain partially degraded or masked versions of the stimuli. When presented with such noisy visual patterns, the subject will tend to make more or less incorrect choices, depending on what parts of the original stimuli have been more heavily altered by the noise. The investigator can then separately process (e.g., average) the noise fields leading, respectively, to the correct and incorrect recognition of the stimuli, so as to obtain saliency maps (known as *classification images*) showing what visual features are diagnostic of the identity of the stimuli. This amounts to infer the perceptual strategies underlying the discrimination of the visual stimuli.

Many different variants of classification image methods have been proposed. One of the most effective to investigate not only human but also animal visual cognition is the so-called *Bubbles method*. Originally introduced by Gosselin and Schyns to study face perception in humans (Gosselin and Schyns, 2001; Schyns et al., 2002), the method has been successfully applied to investigate object recognition in monkeys, at both behavioural (Nielsen et al., 2006b, 2008) and neurophysiological level (Nielsen et al., 2006a; Issa and DiCarlo, 2012), pigeons (Gibson et al., 2005, 2007) and, more recently, rats (Vermaercke and Op de Beeck, 2012; Alemi-Neissi et al., 2013; Rosselli et al., 2015). In its original implementation, the method consists in building opaque masks, punctured by a number of circular, randomly placed, semitransparent openings (the *bubbles*), so that, when one of such masks is applied to a

visual stimulus, only those parts of the stimulus beneath the bubbles are visible. The responses of the subject to the bubble masked stimuli are then processed by dividing the sum of the masks leading to correct identification of a given stimulus by the sum of all the masks applied to that stimulus. The resulting saliency maps reveal what parts of the stimuli are more or less likely to yield a correct classification, when visible through the bubbles — these parts have been named as, respectively, salient and antisalient, with reference to the stimulus identity, by Zoccolan and colleagues (Alemi-Neissi et al., 2013; Rosselli et al., 2015). Various statistical tests, such as Z-scores (Gosselin and Schyns, 2001; Schyns et al., 2002) or permutation tests (Alemi-Neissi et al., 2013; Rosselli et al., 2015) can then be applied to evaluate what proportion of the salient and anti-salient regions is significantly more likely than expected by chance to determine the subject's perceptual choices.

Vermaercke and Op de Beeck (2012) were the first to apply the Bubbles method in a rodent species, with the goal of investigating the perceptual strategy underlying rat discrimination of two geometrical shapes — a square and a triangle. Their implementation of the method departed from the original one in several ways. The rats were tested in a 2-Stim/2-Choices task (see Section 3.2), with both visual patterns being simultaneously shown to the animal on two adjacent computer monitors, rather than a single stimulus per trial being presented, as in Gosselin and Schyns, 2001. The same bubbles masks were applied to both the stimuli, and the bubbles themselves were the occluders, rather than being transparent windows through an otherwise opaque mask, as in Gosselin and Schyns original implementation (2001). By applying this method, Vermaercke and Op de Beeck (2012) found that rats discriminated the two shapes mainly by relying on the lower part of the stimulus display, thus confirming an earlier conclusion of Minini and Jeffery (2006). At the same time, they found that, in trials where the bottom part of the stimuli was largely occluded, rats were still able to extract discriminatory information from the upper portion of the shapes. This led the authors to conclude that rats are capable of using a flexible, context-dependent strategy to process visual object information.

Two studies of Zoccolan et al. followed, where the Bubbles method was applied according to the original design of Gosselin and Schyns 2001, i.e., (1) by presenting one stimulus at the time to the rat, in a 1-Stim/2-Choices task (see Section 3.3); and (2) by randomly placing transparent, circular openings over otherwise opaque masks, having the same colour of the background of the object stimuli. The latter were the complex, multilobed objects that Zoccolan et al. (2009) had previously used to investigate invariant object recognition in rats (see Section 3.3). Also in this experiment, the objects were presented across a range of identity-preserving transformations (size and position changes, as well as in-plane and in-depth rotations). The larger structural complexity of these stimuli, along with the 1-Stim/2-Choices task (see discussion in Section 3.3), yielded patterns of diagnostic features that were much richer than those obtained for the square and triangles by Vermaercke and Op de Beeck (2012). Rats were found to rely on a multifeatural processing strategy, which remained partially invariant under changes of object appearance (Alemi-Neissi et al., 2013). At the same time, the complexity and invariance of rat perceptual strategies were substantially subject- and stimulus-dependent (Alemi-Neissi et al., 2013; Rosselli et al., 2015).

Taken together, the three studies reviewed above illustrate how advanced psychophysical procedures, originally developed to investigate shape processing in humans, can be successfully applied to probe rodent object vision. Thanks to the Bubbles method, it was possible to go beyond previous attempts at understanding rat perceptual strategies, based on applying a limited number of ad hoc manipulations to the visual stimuli (Sutherland and Carr, 1962; Sutherland et al., 1962; Simpson and Gaffan, 1999; Minini and Jeffery, 2006; Brooks et al., 2013). At the same time, the variable complexity of processing strategies reported between and within Bubble studies indicates how sensitive rodent pattern vision is to the specific set of stimuli used by the investigators and calls for further experiments. It also points to the challenge of properly interpreting the results of the Bubbles method that, as most classification approaches, is linear (i.e., it can recover only the linear relationship between stimulus parts and perceptual choices) and produces results that are inherently qualitative (the saliency maps), thus making the quantification of inter-subject differences not trivial. Progress on this front can be achieved by using the classification images to build predictive models of a subject's perceptual choices (Pritchett and Murray, 2015; Neri, 2017), or by combining them with other computational approaches, such as information theory, to infer visual processing mechanisms from behavioural and neurophysiological data at a more quantitative level (Smith et al., 2012; Rousselet et al., 2014; Ince et al., 2015, 2016; Delis et al., 2016).

4.3 Visual Priming Paradigms

Behavioural investigation of visual functions often entails testing the ability of a group of subjects to generalize a previously learned discrimination to novel visual conditions. An example is the test of generalization to transformed appearances of previously learned objects that is typically carried out in studies of visual object recognition

(Zoccolan, 2015). More in general, generalization tests allow understanding to what extent previously unseen visual stimuli are spontaneously perceived by an observer as similar to the stimuli he was originally trained to recognize. This knowledge, in turn, provides a measure of the overlap between the neuronal representations of the trained and novel stimuli, thus yielding key insights about the brain mechanisms underlying the processing of visual information.

Despite their central role in investigating visual cognition, generalization tests are often difficult to implement, and purely perceptual similarity measurements are hard to obtain. This is especially true when testing animal subjects, which requires reward to be delivered to keep their motivation high and, therefore, feedback to be provided about the correctness of their choices. Traditionally, this issue has been circumvented by administering to the subjects *transfer* (or *no-feedback*) trials, where feedback (e.g., reward) is withheld. A recent application of this approach to investigate rodent vision is the study of Zoccolan et al. (2009), where, in a fraction (~11%) of the trials used to test rat generalization to novel object views, neither reward nor timeout was supplied, following rat response. This approach, however, has a few drawbacks. The number of *no-feedback* trials must be limited to a small fraction of the total, so as to prevent the animals from loosing their motivation to respond to the stimuli. This strongly constraints the number of novel stimulus conditions that can be tested under pure generalization. In addition, these conditions are presented in the context of a broader range of stimuli yielding feedback, thus limiting the extent to which true generalization can be tested. For instance, in Zoccolan et al. (2009), only 12 out of 108 object views were presented in no-feedback trials, thus raising the question of whether the extensive training received by the animals with variation in object appearance (i.e., the 108 rewarded views) was necessary for them to succeed also with the 12 not-rewarded views − i.e., it remained unknown whether the rats would be capable of spontaneous generalization to transformed object views, without any previous explicit experience with any object transformation. Finally, it is unclear whether the animals respond to the stimuli shown in no-feedback trials as they would if the stimuli were presented in regular trials − especially if no-feedback trials contain stimuli with unusual appearance, rodents may gradually learn that those images cannot possibly earn them any reward, and they may start ignoring those trials or providing random responses. This could lead to a possible underestimation of their generalization ability.

In studies of human visual perception, an elegant and effective solution to this problem is provided by psychophysical experiments relying on perceptual priming or adaptation after-effects. Priming and adaptation are two well-known perceptual phenomena, where perception of a test stimulus is altered by previous presentation of another stimulus, i.e., the prime or the adapter (Wiggs and Martin, 1998; Clifford and Rhodes, 2005). While the prime has an 'attractive' effect on the perception of the test stimulus (i.e., it renders it perceptually more similar to the prime itself), the adapter has a 'repulsive' after-effect (i.e., it renders the test stimulus perceptually more different from the adapter). Both phenomena have been successfully and extensively exploited to investigate the neuronal representations underlying visual processing in humans (Biederman and Cooper, 1991, 1992; Suzuki and Cavanagh, 1998; Bar and Biederman, 1998, 1999; Leopold et al., 2001; Afraz and Cavanagh, 2008, 2009; Kravitz et al., 2008, 2010). In fact, by measuring the effectiveness of a prime (or adapter) in altering the perception of a test stimulus, it is possible to infer the extent to which the prime/adapter is spontaneously perceived as similar to a previous stimulus the observer may have learnt. In this sense, a typical application is to use priming or adaptation paradigms to test the invariance to transformation (e.g., retinal translation or scaling) of visual perception. A novel, transformed view of a previously learned target object will be able to attract (or repel) the observer's perception of a test object, towards (or away from) the identity of the target object, depending on how perceptually similar the transformed and default (i.e., previously learned) views of the target object are. The magnitude of the priming (or adaptation) will provide an estimate of such perceptual similarity and, as consequence, of the perceptual constancy (i.e., invariance) of the target object under identity-preserving transformations.

While the use of priming or adaptation paradigms is widespread in human vision studies, their application to investigate animal visual perception has been mainly restricted to monkey experiments (Li et al., 1993; Kohn and Movshon, 2004; Sawamura et al., 2006; Leopold et al., 2006; McMahon and Olson, 2007; Verhoef et al., 2008; Liu et al., 2009; Müller et al., 2009; Kaliukhovich and Vogels, 2011). Only one study, to our knowledge, has applied a priming paradigm to investigate visual object recognition in a rodent species (Tafazoli et al., 2012). In this study, the authors first trained a group of rats to categorize a set of visual objects resulting from morphing in different proportions two object prototypes. Such morphed objects formed a continuous shape dimension (whose extremes were the prototypes), along which the authors trained the rats to classify the stimuli according to whether they were closer (i.e., visually more similar) to one prototype or the other. This yielded psychometric curves that served as a reference when, in a second phase of the experiment, either prototype was briefly flashed (for ~50 ms) as a prime, just before presentation of a morphed object (the inter stimulus interval was set to 66 ms). The prime stimulus produced

a shift/compression of the whole psychometric curve in a direction that was consistent with the rat becoming biased to report the identity of the prime itself more frequently. Critically, this shift was caused not only by the default views of the prototypes but also when the prototypes underwent a range of identity-preserving transformations (i.e., translations, size changes, in-depth rotations, and their combination) that the animals had never seen before. The magnitude of the priming (measured as the area between the psychometric curves obtained in regular and prime trials) provided an estimate of how perceptually similar the default and transformed views of the prototypes were for the rats. Overall, a significant priming was observed for most transformations, with a magnitude that was inversely related to the magnitude of the resulting change in object appearance (e.g., larger rotations from the default pose led to progressively smaller priming).

So far, the experiment reviewed above is the only example of application of a visual priming paradigm to probe rodent visual perception. However, the success of Tafazoli et al. (2012) in isolating the purely spontaneous (perceptual) component of transformation-tolerant recognition indicates that approaches based on visual priming and, possibly, adaptation aftereffects could play, in rodent visual studies, a role as important as the one they have been playing in primate studies. For example, a priming paradigm similar to the one used by Tafazoli et al. (2012) could be exploited to investigate whether rodents are capable of high-level integration of motion signals − a question that was investigated by some recent neurophysiological studies (Juavinett and Callaway, 2015; Palagina et al., 2017), but that has never been explored at the perceptual level.

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