

Mateus Torres Cruz

Orienting of visual selective attention
following auditory cues, in rats

Orientação da atenção seletiva visual por
pistas auditivas em ratos

São Paulo

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Ph.D. Thesis presented at the University
of São Paulo, Institute of Biosciences,
Brazil, to obtain the title of Doctor of
Sciences. Concentration area: General
Physiology.

Advisor: Gilberto Fernando Xavier

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Dedication

*To my nuclear family–
Conceição, Deraldo and Simão –
for inspiring me to follow this path
and for doing their best to give me
all the support I needed to succeed.*

*To my spiritual brother – Natan – for
taking and throwing many
punches for and with me.*

*To my spouse – Zeni – for
helping me become a better human
being.*

*To my master – Jesus – for
teaching me how to live.*

*To God, for allowing me to be
co-creator of myself.*

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*A minha família nuclear –
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me inspirarem a seguir este
caminho e por fazerem o melhor
que puderam para me dar todo o
suporte que eu precisava para
vencer.*

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melhor.*

*Ao mestre – Jesus – por me ensinar
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cocriador de mim mesmo.*

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Although that sentence is true, it did not seem enough as an acknowledgement.

After giving it some thought, and reading other acknowledgements of other people, I realized that there is something unique about thanking people by name. Our names act as a unique identifier for our identities, such that saying or writing a person's name makes direct reference to all that person represents in the real world. So by thanking someone by name, I would not only be acknowledging that the effort the person made to help me finish my work was crucial to me, but saying that that person was essential for me to be where I am; and that feels powerful.

Besides that, although this work is not a part of me, it is a product of who I am. It is what it is because I became who I needed to be to complete it, and I would not be who I am today without the help of many people.

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Epigraph

*To live is to learn; and to learn is to
try to live better."*

(Nyerere, J. K. (1973). Adult
education year. *Freedom and
development*. p. 138)

Abstract

Cruz, M. T. (2022). Orienting of visual selective attention following auditory cues, in rats (Ph.D. Thesis). Institute of Biosciences, University of São Paulo, São Paulo.

Orienting of **selective attention** is a widely studied phenomenon in the Neurosciences. Studies in both humans and non-human animals, employing a wide range of methods – from behavioral tasks, to optogenetic manipulations –, have advanced the knowledge in the area. Thanks to these advances two main types of orienting of attention have been describe, **endogenous orienting**, which depend on the internal expectations of the animal about its environment, and **exogenous orienting**, which depends on how salient environmental stimuli are. Although important advances have been made, the understanding of both the phenomenology and physiological underpinnings of selective attention is far from complete. Animal models in biological studies have historically allowed great leaps forward for scientific knowledge. The present work adds to the field of attention by further investigating the use of in rats in the study of attention. Specifically, by using a behavioral task – a Posner-like covert orienting of attention task using auditory cues and visual targets – we investigated select attention shifts between two different sensory modalities, i.e., vision and hearing. In Experiment 1 experimentally demonstrated, for the first time, that exogenous orienting of visual attention by auditory stimuli is possible in rats. Experiment 2 investigated how exogenous and endogenous orienting are affected by whether visual and auditory stimuli are presented at the same or at different locations, i.e., by their degree of spatial superposition. The results show that the intermodal attentional shift does not seem to depend on presentation of the auditory cue and visual target exactly in the same location. By bringing to light these previously unknown aspects of the orienting of attention in rats, this study contributes to the use of this animal model in future investigations of the physiological underpinnings of attention.

Palavras-chave: Posner task, Covert orienting of attention task, Operant conditioning, Mental chronometry, Spatial orienting.

Resumo

Cruz, M. T. (2022). Orienting of visual selective attention following auditory cues, in rats (Ph.D. Thesis). Institute of Biosciences, University of São Paulo, São Paulo.

A orientação da atenção seletiva é um fenômeno amplamente estudado nas Neurociências. Estudos em humanos e animais não humanos, empregando uma ampla gama de métodos – desde tarefas comportamentais, até manipulações optogenéticas –, têm ampliado o conhecimento na área. Graças a esses avanços, dois tipos principais de orientação da atenção foram descritos, a orientação endógena, que depende das expectativas internas do animal sobre seu ambiente, e a orientação exógena, que depende de quão salientes são os estímulos ambientais. Embora avanços importantes tenham sido feitos, a compreensão tanto da fenomenologia quanto dos fundamentos fisiológicos da atenção seletiva está longe de estar completa. Modelos animais em estudos biológicos têm, historicamente, permitido grandes avanços no conhecimento científico. O presente trabalho contribui para o campo da atenção, investigando o uso de em ratos no estudo da atenção. Especificamente, usando uma tarefa comportamental – uma tarefa de orientação encoberta da atenção do tipo Posner, usando pistas auditivas e alvos visuais – investigamos deslocamentos da atenção seletiva entre duas modalidades sensoriais diferentes, i.e., visão e audição. O Experimento 1 demonstrou experimentalmente, pela primeira vez, que a orientação exógena da atenção visual por estímulos auditivos é possível em ratos. O Experimento 2 investigou como a orientação exógena e endógena é afetada por estímulos visuais e auditivos serem apresentados no mesmo local ou em locais diferentes, ou seja, pelo seu grau de superposição espacial. Os resultados mostram que o deslocamento da atenção intermodal parece não depender da apresentação da pista auditiva e do alvo visual exatamente no mesmo local. Ao trazer à luz esses aspectos até então desconhecidos da orientação da atenção em ratos, este estudo contribui para o uso deste modelo animal em futuras investigações das bases fisiológicas da atenção.

Palavras-chave: tarefa de Posner, tarefa de orientação encoberta da atenção, condicionamento operante, cronometria mental, orientação espacial.

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List of Acronyms

ANOVA	Analyses of Variance
GLMM	General Linear Mixed Models
IOR	Inhibition Of Return
IQR	interquartile range
ITI	Inter-Trial Interval
LED	Light-Emitting Diode
MT	Movement Time
NP	Non-Predictive
OCC	Operating Conditioning Chamber
P	Predictive
RT	Reaction Times
SEM	Standard Error of the Mean
SOA	Stimulus-onset asynchrony

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1 Introduction

At every moment of our everyday lives, we are continuously facing countless sensory stimuli. As only a portion of them is relevant, the ability to focus only on the most relevant stimuli at each time is crucial to behave optimally. This capacity must also be flexible because a stimulus that is important in a given context might not be in another. For example, traffic lights are extremely important when one is driving a car, but not important when one is having a conversation in a nearby coffee shop. This flexible and selective ability of either filtering out or enhancing certain stimuli depending on the context is called selective attention, or simply attention.

William James, the father of Northern American psychology, was one of the first to scientifically investigate this phenomenon. In his “The Principles of Psychology” he summarizes the nature of attention in a quote that has already become a classic in the field:

Everyone knows what attention is. It is the taking possession by the mind in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought....It implies withdrawal from some things in order to deal effectively with others. (James, 1890)

This quote illustrates an important aspect of attention: the fact that it can be voluntarily oriented (“taking possession by the mind in clear and vivid form”) towards specific “objects or trains of thought”. This is called **endogenous orienting** and is how we direct attention when reading a book or while looking for someone wearing a red hat in a crowd. Attention, however, can also be “caught” automatically by salient features, like strong colors, movements, flashing lights. This is what happens when someone suddenly barges in through a door of a room we are in or when someone blows a horn near you in traffic. In this case, **exogenous orienting** is captured without direct influence of volition. These two different ways of directing attention interact constantly, allowing us to keep our mental resources, which are limited (see Carrasco, 2011), in what is important for our current goals while also keeping track of sudden events that might be important.

1.1 HOW ATTENTION HAS BEEN INVESTIGATED?

In 1980, Michael I. Posner, a Northern American psychologist, described a novel behavioral task, the covert orienting of attention task (Posner, 1980), that allowed the detailed investigation of these types of orienting and that still is very influential on how attention is experimentally studied to these days. By using it, he showed that selective attention could be investigated in humans by using a visuospatial task in a computer screen.

In a typical Posner task (see Chica et al., 2014 for a review) the subjects are exposed to several trials in a session. In each trial their goal is to, whilst maintaining their eyes fixated at the center of the screen, report the appearance of a visual stimulus, referred to as “**target**”, by pressing a button. These targets occur randomly in predetermined areas of the screen, typically to the left or right of the fixation point. Critically, before the target appearance, a different visual stimulus, hereinafter referred to as the “**cue**”, is presented, which provides information about the future location of the target. These cues may be **valid**, when they correctly indicate target location, or **invalid**, when they incorrectly do so. Posner and many other authors showed that targets preceded by valid cues generate shorter Reaction Times (RTs) and greater accuracy when compared to targets preceded by invalid cues, indicating that the subjects oriented attention towards the place indicated by the cue, responding faster and more precisely when this information led them to the correct target location (e.g. Bartolomeo et al., 2007; Berger et al., 2005; Carrasco, 2011; Dragone et al., 2017; Folk et al., 1992; Jonides, 1981; Juola et al., 2000; Luck et al., 1996; Martín-Arévalo et al., 2013; Meyberg et al., 2015; Posner, 1980). Differences in RTs (RT in invalid trials “minus” RT in valid trials) are usually referred to as “**validity effects**” and its magnitude can be used as a proxy of the influence of attention on the task being.

The most important feature of this task is that it allows studying orienting of attention independently from the movement of the sensory surfaces – the eyes, in this case. This is why it is called a **covert attention** task, in opposition to **overt attention** tasks, where there is concomitant orienting of sensory surfaces and attention (Luck & Vecera, 2002; MacInnes et al., 2020). By controlling the position of the sensory receptors, the covert task allows ascribing any effects to attention shifts and not to changes in sensory reception. Thanks to these characteristics, this task gained

widespread popularity, enabling important advances not only in the investigation of visual attention (see Carrasco, 2011 for a review), but also in auditory attention (e.g., McDonald & Ward, 1999; Mondor & Zatorre, 1995; Spence & Driver, 1994), tactile attention (e.g., Spence & Gallace, 2007; Tassinari & Campara, 1996) and also in the study of cross-modal attention shifts (e.g., Spence et al., 2000; Störmer, 2019; Tassinari & Campara, 1996).

The task allows fine-tuned assessment of different aspects of attentional orienting, including its time course, predictability of the pending events and types of cues.

The **Stimulus-Onset Asynchrony** (SOA), in this task, is the time interval between the cue onset and the target onset, such that a SOA of 0 ms means that both stimuli are presented simultaneously and a SOA of 1000 ms means that the onset of the cue precedes the onset of the target by 1000 ms. As one may suppose, it is possible to investigate the time course of orienting of attention by measuring the reaction time to the target and accuracy of performance using different SOAs (e.g., Z. Wang & Theeuwes, 2012). It is often assumed that SOAs shorter than 50 ms rarely elicit any validity effects in humans, and that longer SOAs do it. This delay in the appearance of validity effects would reflect the time required for engaging attention. Thus, when cue and target occur too close in time there is not enough time to shift the focus of attention. The way orienting of attention affects perception after these ~50 ms depends on both predictability and type of cue (see below).

Predictability refers to the likelihoods the cue informs either validly or invalidly the pending target location. When exposed to a **predictive** scheme, i.e., the percentage of valid trials is greater than that of invalid trials (e.g., 80 % valid and 20 % invalid), subjects trend to “trust” the information brought by the cue and orient spatial attention accordingly. When exposed to a **non-predictive** scheme, with the same percentage of valid and invalid trials (i.e., 50 % valid and 50 % invalid), subjects tend to “ignore” the cues, at least relative to spatial signaling, since the cues do not bring any relevant spatial information about the pending target location. Therefore, it seems natural to suppose that predictive schemes generate validity effects. In fact, this occurs in most of times. However, this does not necessarily mean that non-predictive schemes do not induce validity effects, since this depends largely on the type of cue.

Different types of cues, including symbolic and peripheral, have been used to investigate selective attention. **Symbolic** cues correspond to arbitrary symbols which

meaning is acquired through learning. Any symbol can be used. For instance, high-pitched beep could mean left and a low-pitched beep mean right; a square could indicate left and a circle indicate right; an “A” letter could mean left and a “B” letter could mean right; and so on. **Peripheral** cues, on the other hand, are salient stimuli which appearance, by itself, capture attention independently on the likelihood of indicating or not the pending target location. These type of cues come in many shapes and forms and usually occur in the immediate vicinity of the target. A classical visual example is the thickening of a peripheral box inside of which the target appears (e.g., Luck et al., 1996). Sounds with identifiable origin have also been used as peripheral cues (e.g., Hillyard et al., 2016; Störmer et al., 2009).

Combinations involving cue types, predictability schemes and SOAs have contributed for distinguishing different forms of orienting of attention.

For instance, in a covert orienting of attention task using symbolic auditory cues, a bilateral low-pitched beep indicates that a pending visual target, e.g., bright dots, may appear in the left visual field, and that a bilateral high-pitched beep indicates that the pending visual target may appear in the right visual field. Here, the cue is symbolic because its meaning has to be acquired (note that the association could be the reverse, i.e., low-pitch indicating right and high-pitch indicating left). If a non-predictive scheme (i.e., 50% of trials are valid and 50% of trials are invalid) is implemented using this type of cue (which spatial source is unidentifiable), no validity effect would be found. This is related to the fact that symbolic cues require learning in order to allow orienting of attention and, as the non-predictive scheme presents no pattern between cue presentation and pending target location, there is no association to be learned and, thus, no attentional effects are found (Jonides, 1981; Luck & Vecera, 2002).

Differently, a predictive scheme using symbolic auditory cues and visual targets should produce validity effects, since there would be a consistent pattern between the beeps and the location of dots. For instance, a high-pitched beep preceding a bright dot on the left in most trials, would allow, after some trials, prediction about the pending target location and thus orienting of attention to the cued side. This would render response to the target faster and more precise when the cue is valid, as compared to when it is invalid. This improved performance in valid trials is sometimes called **facilitation**. It has been considered an **endogenous** orienting of attention because it depends on the subjects' internal expectations about the meaning of the stimuli, which

is formed through learning (Chica et al., 2014; Luck & Vecera, 2002). These validity effects usually begin around SOAs of 150 ms and last for several seconds (Doallo et al., 2004; Posner, 1980; Remington & Pierce, 1984; Shulman et al., 1979).

Another possible combination of cues and targets may involve peripheral auditory cues, for instance either low-pitched or high-pitched beeps, laterally and randomly presented close to the location where the visual target later appears. Differently from the symbolic non-predictive cues, peripheral stimuli do generate validity effects even when half of the trials are valid and the other half are invalid (i.e. they are non-predictive). Presentation of the cue peripherally, near the location of the pending target, captures attention in an **exogenous** manner (Chica et al., 2014; Luck & Vecera, 2002). This facilitation effect appears at SOAs shorter (of about 50 ms) than those observed for endogenous orienting of attention, leading to the interpretation that exogenous orienting of attention is quicker. This exogenous capture of attention, however, seems transient and last for about 100 ms, waning shortly after. Therefore, peripheral non-predictive cues seems to promote “automatic” capture of attention due to cue saliency, showing facilitation effects at short SOAs (Posner & Cohen, 1984; Wright & Richard, 2000). Interestingly, under certain circumstances, non-predictive peripheral cues associated with longer SOAs (about 300 ms) may reverse the validity effect, i.e., reaction times in trials using invalid cues are shorter as compared to those seen in trials using valid trials (Posner & Cohen, 1984; Wright & Richard, 2000). This effect, known as **Inhibition Of Return (IOR)**, demonstrated both for cues and targets of the same sensory modality and cues and targets of different sensory modalities (Spence et al., 2000; Spence & Driver, 1998), is thought to promote attention orienting towards novel spatial locations by inhibiting orienting towards recently attended locations (Martín-Arévalo et al., 2013).

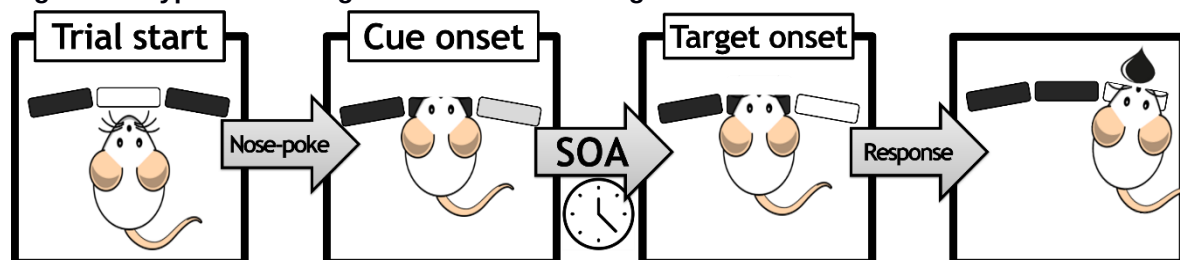
Finally, peripheral cues associated with predictive schemes promote, as expected, facilitation effects at short SOAs related to capture of exogenous attention by peripheral cues, and also endogenous orienting of attention at longer SOAs, associated with the predictability of the scheme (Bartolomeo et al., 2007; Luck & Vecera, 2002).

1.2 THE USE OF RATS IN THE INVESTIGATION OF ATTENTION

The Posner task has been adapted for non-human primates (Bowman et al., 1993), fish (Gabay et al., 2013), chicken (Sridharan et al., 2014), mouse (Li et al., 2021; L. Wang & Krauzlis, 2018) and rats (Rosner & Mittleman, 1996; Ward & Brown, 1996). These adaptations have allowed further investigations on the mechanisms and neural substrates of attention in ways not possible with humans.

Rats have been widely employed as experimental models in science, mainly due to their relative similarity to humans, small size, ease of maintenance, short life cycle, and relatively complex behavioral repertoire (Aitman et al., 2016; Ellenbroek & Youn, 2016). It is not surprising, therefore, that it was one of the first animal models to be adapted to attention research. The Posner task for rats involves an operant conditioning chamber (OCC) with at least three holes in a wall, each hole equipped with a light source on its end (see Figure 2 for more details); these holes serve as “fixation point” (central hole) and targets (lateral holes). A typical trial (Figure 1) involves the animal nose-poking the central hole, receiving a visual cue (a dim light) through the lateral holes, keeping the nose poke for a SOA and then making a lateralized response to the target (a bright light) presented in one of the lateral holes (Rosner & Mittleman, 1996; Ward & Brown, 1996).

Figure 1 – Typical trial stages in a covert orienting of attention task in rats.



Source: Mateus Torres Cruz.

Early studies with rats employing the adapted Posner task investigated the role of different brain regions, or neurotransmitter systems, on orienting of attention, including the parietal posterior cortex (Rosner & Mittleman, 1996; Ward & Brown, 1997), striatal dopamine (Ward & Brown, 1996), thalamic reticular nucleus (Weese et al., 1999), cholinergic neurotransmission (Phillips et al., 2000) and the subthalamic nucleus (Phillips & Brown, 2000). Even though none of these studies investigated the phenomenology of attentional orienting, data allowed evaluation of hypothesis related

on how rats orient attention. Collectively, these studies suggest that rats, similarly to humans, exhibit validity effects when exposed to the task, responding faster and more accurately in valid trials, as compared to invalid trials. Further, when the peripheral cues were non-predictive, validity effects did not appear at SOAs longer than 400 ms (Phillips et al., 2000; Weese et al., 1999), whilst validity effects for predictive cues extended to SOAs up to 1500 ms (Rosner & Mittleman, 1996; Ward & Brown, 1997).

Marote and Xavier (Marote & Xavier, 2011) were the first to directly investigate the phenomenology of attentional orienting in rats. Their results corroborated previous hypotheses that predictive cues tend to generate facilitation at longer SOAs, as compared to non-predictive cues. These authors suggested that, similarly to humans, rats exhibit short-lived validity effects for peripheral non-predictive cues interpreted as exogenous orienting of attention and more persistent validity effects for peripheral predictive cues interpreted as “endogenous-like” orienting of attention. They did not risk to refer to this latter effect as properly endogenous because when using peripheral cues, exogenous effects are always present which may confound with endogenous orienting of attention at intermediate SOAs. To have an unequivocal answer related to endogenous orienting of attention in rats, it would be necessary to employ symbolic predictive cues, that do not capture exogenous attention.

In order to evaluate the effectiveness of symbolic cues for promoting orienting of endogenous attention in rats, a task using auditory cues and visual targets was implemented (Cruz, 2017). In contrast to previous studies where dim lights were used as visual cues, in this novel task pure-tone sound beeps with different frequencies were employed as symbolic auditory cues. When beeps predicted the location of the visual target, there were validity effects. In other words, when a high-pitched beep preceded a visual target to the right in 80% of trials and a low-pitched beep preceded a visual target to the left in 80% of trials, subjects improved their performance (there was a reduction in reaction times and an increase in accuracy) in valid trials as compared to invalid trials¹. Differently, when beeps were presented non-predictively to a different group of animals, no validity effects were seen. These results showed that rats do orient attention in a purely endogenous manner.

¹ The frequency of the beeps and the side they indicated for the impending visual target were counterbalanced, such that it is not possible to explain the results solely based on the frequencies employed.

1.3 THE SCOPE OF THIS WORK

Our previous study (Cruz, 2017) also included independent groups of subjects exposed to predictive and non-predictive peripheral auditory cues. While validity effects were seen for subjects exposed to peripheral predictive cues, there were no validity effects for subjects exposed to peripheral non-predictive cues. Together, these results suggested that peripheral auditory cues do not lead to capture of visual attention exogenously. Since results involving validity effects when using either symbolic or peripheral auditory cues were very similar, the observed validity effects were all ascribed to endogenous orienting of attention.

Some hypotheses were advanced for the lack validity effects when using non-predictive peripheral auditory cues. First, that rats are not able to orient visual attention exogenously when the cues are auditory. Second, that the location of the beep-releasing speakers relative to the location of the nose-poke device where visual targets were presented were to distant in space, thus limiting the occurrence of validity effects.

The first explanation seems farfetched, since identification of the origin of sounds is supposed to play an important role in orienting towards visual stimuli in mammals (R. S. Heffner & Heffner, 1992). The second hypothesis seemed more likely.

Hypothetically, several factors may have contributed for the lack of validity effects when using peripheral non-predictive auditory cues. For instance, the SOAs employed (200, 400, 800 and 1200 ms) may have not been short enough to allow detection of exogenous capture of attention, which usually is detectable at shorter SOAs (see above). It is possible that exogenous attention was captured by the non-predictive auditory cue, but, because of its transient nature, this attentional effect had dissipated at the SOAs employed. Another possible factor may be related to prolonged practice. Human beings exposed to this type of task exhibit reductions of attentional effects (Lupiañez et al., 2001; Weaver et al., 1998). If a similar overtraining phenomenon occurs in rats, this may have contributed for the lack of validity effects because the animals had been exposed to more than 50 testing sessions. The last factor may be related to a possible spatial dissociation between the cue and target, an effect known to reduce attentional effects in humans (Spence, 2013). That is, the beep sounds were released from speakers located laterally to the place where the visual

targets were presented (see Figure 3). This supposed spatial dissociation could have diminished the validity effect. Perhaps releasing both the cue and the target from the same location, i.e., inside the hole where the visual target was presented, could increase the validity effect.

This thesis reports two experiments that aimed at evaluating these hypotheses.

Experiment 1 evaluated if cross-modal, auditory-visual exogenous orienting of attention using peripheral non-predictive cues associated with shorter SOAs promotes the appearance of the validity effect in rats. That is, the two initial factors discussed above were evaluated by exposing the subjects to shorter SOAs and by reducing the amount of repetitive training. Results confirmed that rats do exhibit validity effects when orienting attention to visual targets using auditory cues, in a manner consistent with exogenous orienting of attention.

Experiment 2 investigated if a closer spatial origin of auditory cues and visual targets contributes for increasing the validity effect. Although this hypothesis was initially raised because of the lack of exogenous orienting of attention for non-predictive peripheral cues (Cruz, 2017), the experiment aim was broader. In addition to evaluating exogenous orienting of attention by non-predictive peripheral stimuli when cue and target have the same spatial origin, endogenous orienting of attention was also investigated using predictive peripheral auditory cues. A possible prediction was that a closer spatial auditory cue and visual target origin would enhance the validity effect, similarly to what happens in humans (Spence, 2013; Spence & McDonald, 2004). Surprisingly, we found that this closer spatial cue and target proximity had little or no effect in orienting of attention in rats.

2 Objectives

The general goal of this study was to investigate to which extent rats employ auditory cues to orient spatial visual attention. Taking into account previous hypotheses advanced by Cruz (2017), described above, our specific objectives included:

1. Investigate the time course of orienting of attention, particularly at short time intervals (SOAs < 300 ms), when using peripheral non-predictive auditory cues and visual targets;
2. Evaluate attentional effects in rats when using a conditioning protocol that avoids prolonged practice with task stimuli, and;
3. Test to which extent a closer spatial origin of auditory cues and visual targets stimuli interfere with either endogenous or exogenous orienting of attention, employing peripheral predictive and non-predictive auditory cues in independent groups of subjects.

6 Conclusions

The main contribution of this study was the demonstration that rats are able to orient visual attention exogenously when preceding auditory peripheral cues are presented in a Posner-like task adapted to rats.

This intermodal attentional shift does not seem to depend on presentation of the auditory cue and visual target exactly in the same location, since similar effects were observed with and without their spatial superposition.

Attentional effects in rats, similarly to humans, is affected by repetitive training, such that repeated exposure to the task stimuli wanes attentional effects.

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