“We are not students of some subject matter, but students of problems. And problems may cut right across the boundaries of any discipline.”

- Karl Popper

“The best way to know a thing is in the context of another discipline.”

- Leonard Bernstein

Content

Foreword

Dear reader,

As the (temporary) senior advisor, I have the pleasure to introduce to you this new issue of the Journal of Neuroscience & Cognition. I've seen the work in progress by the contributors and I am surprised by the motivation and engagement with which the team put this edition together.

This time, the main focus is on interdisciplinarity, something that does not always seem to have priority in the academic environment. Of course, money is key here; working together also means sharing the costs and benefits, which is sometimes hard in terms of intellectual property and grant applications. However, while some might have the tendency to work alone, the lack of interdisciplinarity might result in a tunnel-vision and will leave the bigger pictured covered.

For example, if one asks a scientist to explain the mechanisms that drive some sort of behavior, the answer will probably depend highly on the specific research domain of the researcher. A molecular biologist might explain the behavior in terms of fine grained interactions at the cellular level, while the cognitive psychologist might explain the same behavior in terms of cognitive constructs and underlying brain systems. In all, both scientists observe the same behavior and translate this into their own terminology. That being said, interdisciplinarity is not only the key to the bigger picture, it is also the glue that connects different scientific domains, necessary to translate between them. The current issue of the Journal of Neuroscience and Cognition will show that there are many attempts that prove interdisciplinarity to be an important factor in neuroscience.

All the best,

Martijn Mulder, PhD
Senior supervisor Journal of Neuroscience & Cognition

Editorial

Dear reader,

Before you lies the second issue of the Journal of Neuroscience and Cognition 2019. The topic of this issue has been kept a secret for you, which was very challenging due to our excitement. To tackle challenges in society and healthcare through research, the engagement of many disciplines is required. Disciplines that wire together, fire together – this is what we wanted to portray.

In this journal on Neuroscience: the crossroads of disciplines, we sought to give insight into different disciplines working together in order to improve knowledge and care in the multifaceted scope of neuroscience. Guus van Loon, Freek Hoebeek, Jeroen Dudink, Elly Hol and Sarah Durston, all working in different research fields of neuroscience, give their views and wisdom on the importance of interdisciplinarity and teamwork. Furthermore, we have summarized the ten most cited articles from the journal, 'Neuroscience', for you. The articles are distinct from each other, but all have the same aim: explaining brain and behavior.

From your fellow students, this journal includes a very interesting article by Arne, and two reviews written by Lieke and Marit. Furthermore, it includes a methodology section written by Ben Harvey on MRI, and views on doing a PhD in research as a trained medical doctor by Katherine Tan. We again have a very interesting book review, adventures abroad by two second year students, and some perspectives on career outcomes after the master. Jesca wrote about her experiences at the Dutch Neuroscience Meeting, and the Mind the Brain committee wrote about the challenges they faced while organizing the conference this year.

We hope you enjoy reading this journal, and wish you the best for the upcoming academic year!

Yours sincerely,

Ilse van Rijssen
Editor in Chief

Eye hear you

The effect of the pre-saccadic shift of attention on auditory spatial perception

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In our natural environment in which we are constantly bombarded with sensory information, spatial attention enables us to select only the most relevant stimuli for further processing. Where we look at indicates where spatial attention is directed. Previous studies extensively showed that shifts of attention towards saccade targets precede the saccades that we make. Additionally, saccades do not only direct visual attention, but auditory attention as well. Previous research has shown that the direction of an upcoming saccade affects how fast we are in detecting auditory stimuli. However, whether a planned eye movement affects a more characteristic form of auditory perception, such as localisation accuracy as well, has not been demonstrated yet. The present study investigated whether the pre-saccadic shift of attention affects localisation accuracy in an auditory localisation task. Two cross-modal spatial cueing (exogenous/endogenous) experiments were designed in which visual cues (saccade targets) were presented peripherally. Auditory targets were presented pre- and post-saccadically and subjects' localisation accuracy was quantified. Results demonstrate higher localisation performance when auditory targets were presented at the same side as visual cues with better localisation performance in the vicinity of the saccade destination. When targets were presented pre-saccadically, performance increased as the delay between target presentation and saccade onset decreased. This temporal effect was only demonstrated for exogenously cued saccades. Shifts of spatial attention most frequently occurred around 100 milliseconds preceding saccade execution. Taken together, the results provide evidence for an attentional benefit of saccades in a core characteristic of auditory perception.

Keywords: *Spatial attention; Eye movement; Auditory localisation; Cross-modal; Spatial cueing*

In everyday life during wakefulness, we are constantly exposed to great amounts of sensory stimuli. In order to be able to deal with this, only the most relevant information is selected for further processing. The cognitive function that allows us to make these selections is called "attention". Attention seems to be independent of sensory domain, since - when attention is directed to a certain location in space - sensory information of all senses is strengthened (Driver & Spence, 1998; Mazer, 2011; Wahn & König, 2015). Attention that is directed to a certain location in space is also known as spatial attention (Farah et al., 1989).

Humans are known to be visual animals. We have evolved in such a way that we mainly depend on our eyes when spatially orienting ourselves in the environment, because our visual system provides us with the most detailed spatial information of our surroundings (Cornsweet, 2014). This fact is one of the reasons why we make quick ballistic 'jumps' in eye position, also known as saccades (Ibbotson & Krekelberg, 2011). Once an object is brought into our fovea, we are able to inspect it in much more detail than before, due to the higher density of photoreceptors in the fovea relative to other areas of the retina (Ibbotson & Krekelberg, 2011). This is the reason why our attention is generally directed at our focal point. The focus of attention coinciding with the movement of the eyes is also known as overt attention (Carrasco, 2011; Onat, Libertus & König, 2007). However, attention is also shifted without changing eye position. This is known as covert attention and it can be either voluntary or involuntary (Carrasco, 2011; James, 1910; Posner, 1980). In the literature on saccades, it has been extensively demonstrated that the shift of attention that goes along with saccade execution precedes the moment of saccade initiation. This is considered to be an involuntary form of covert attention, also known as the pre-saccadic shift of attention (Deubel & Schneider, 1996; Godijn & Pratt, 2002; Kowler et al., 1995).

The pre-saccadic shift of attention has been studied extensively since its existence was first demonstrated by Deubel and Schneider (1996). Most studies focused on how this shift of attention affects visuospatial perception at the saccade-end location. Deubel and Schneider (1996), for instance, demonstrated that changing the end location of an upcoming saccade affects how well we are able to discriminate between two similar symbols. They showed that the ability to recognize pre-saccadically presented objects is limited to the intended saccade

target position, with optimal performance when the location of the object that has to be identified matches the intended saccade endpoint. Deubel and Schneider also demonstrated that discrimination performance declines steeply when saccade target and discrimination target are at different locations. Godijn and Pratt (2002) chose a somewhat different approach on studying the effect of the pre-saccadic shift of attention on visuospatial perception. In their study, subjects had to execute a saccade to a certain location and subsequently identify the orientation of a visual target. Godijn and Pratt (2002) used central arrows pointing either left or right to direct saccades, which means that saccades were endogenously (i.e. top-down or voluntarily) cued, rather than exogenously (i.e. bottom-up or involuntarily) (Jonides, 1981). Prior to saccade execution, a prime (visual cue) was presented that was either congruent or incongruent with the target location. Larger priming effects were shown when primes were presented at the saccade destination compared to a no-saccade location. This indicates that a shift of attention also takes place preceding endogenous saccades (Godijn & Pratt, 2002).

Since spatial attention is thought to be independent of sensory modality, one would expect that effects of the pre-saccadic shift of attention would be found in other sensory domains in addition to the visual as well, such as the auditory domain. A study conducted by Rorden and Driver (1999) focused on whether the principle of the pre-saccadic shift of attention also applies across sensory modalities, instead of only within. They studied whether upcoming saccades trigger shifts in auditory attention in the same way as they do for visual attention. Rorden and Driver used an auditory elevation judgment-paradigm to investigate auditory spatial attention, a methodology employed by Spence and Driver (1994) in which participants need to judge the pitch height of a series of sounds that are presented to them. With this paradigm, it was demonstrated that auditory elevation judgments are faster for sounds presented on the side that is exogenously covertly attended.

Rorden and Driver (1999), however, were interested in the potential impact that upcoming saccades might have on auditory attention, and tested whether planning and executing a saccade towards one side produces better auditory elevation judgments on that side compared to the other side. Their results showed that auditory performance is affected by the direction of an upcoming saccade, with better detection performance in the vicinity of the saccade destination. The main advantage of using a speeded discrimination task to measure auditory performance is that it provides a sensitive measure for the distribution of auditory attention. However, a weakness of Spence & Drivers' paradigm is that outcomes might reflect general influences of saccades on reaction times, instead of effects on the core characteristics of auditory perception. Whether saccades' effect on auditory perception exceeds speeded discrimination tasks and reaches core characteristics of auditory spatial perception, such as localisation accuracy, as well is still unclear.

Although the majority of studies on auditory spatial attention have used speeded sound discrimination performance as a measure of auditory perception (Blurton, Greenlee & Gondan, 2015; Lee & Spence, 2017; Spence & Driver, 1994), some studies have demonstrated cross-modal cueing effects of the visual domain on auditory spatial perception in an auditory localisation task as well (Razavi, Oneill & Paige, 2007; Schmitt, Postma & De Haan, 2001). Schmitt, Postma, and de Haan (2001) conducted a study investigating sound discrimination and localisation, and tested how visual cues affect auditory perception and vice versa. Results demonstrated that both auditory and visual location cues guide attention in processing targets from the other sensory domain. Their prime result was a cue-target distance effect, which further characterizes the cross-modal links between the attentional subsystems. Although the findings of Schmitt et al. (2001) seem to suggest a possible effect of the pre-saccadic shift of attention on auditory perception in an auditory localisation task, this effect has yet to be demonstrated. Combining the findings of Rorden and Driver (1999) and Schmitt et al. (2001), the current study investigates whether the pre-saccadic shift of attention affects localisation accuracy in an auditory localisation task. In order to answer this question, we designed a cross-modal spatial cueing experiment. Visual cues were presented in the periphery to direct saccades, because this is most similar to the way in which we make saccades in everyday life. Auditory targets were presented in the horizontal dimension. First, it will be investigated whether same side cue-target presentations result in higher localisation accuracy scores compared to cases in which cue and targets are presented at opposite sides (for further details, see the paradigm of Rorden & Driver, 1999). Additionally, this will be the first study to investigate how an upcoming saccade influences auditory spatial perception over the pre-saccadic timespan and answer the question whether localisation accuracy increases when saccade execution gets closer in time. Lastly, if a target congruence effect is present, we will study the focality of attention shifting towards the intended end location of an upcoming saccade. Assuming that the cross-modal cueing effect, as shown by Rorden and Driver (1999), is not restricted to auditory spatial discrimination, we hypothesized that 1) localisation performance is better when cue and target are presented at the same side (i.e. congruent) compared to opposite sides (i.e. incongruent), 2) performance generally increases over the pre-saccadic interval and 3) benefits of visual cues gradually decline as distances between visual cue and auditory target increase (Rorden & Driver, 1999; Schmitt et al., 2001).

EXPERIMENT 1 - EXOGENOUS CUEING

METHODS

Participants

Twenty-two healthy adults (12 female, 10 male; mean age 23.9 years) took part in this experiment and received twelve euros for their participation. Three participants were excluded due to eye-tracking issues, resulting in a final dataset consisting of nineteen participants (9 female, 10 male; mean age 23.7 years). All subjects reported normal or corrected-to-normal vision and hearing. All subjects were naïve to the exact purpose of the experiment. The experiment took approximately 90 minutes to complete and was approved by the faculty committee of Utrecht University.

Apparatus and materials

The experiment was conducted in a darkened room (509 x 255 x 282 cm), using Python (version 2.7.3) with toolbox PyGaze (WinPython PyGaze 0.5.1). Subjects were seated on a chair that was located exactly in the middle of the width of the room. The subject's head was fixated by a custom-made chinrest to make sure that involuntary head movements during the measurements were minimized. Two broadband loudspeakers (Harman/Kardon, frequency response: 90-20.000 Hz, model number: HK206) were situated in front of the participant, evenly separated laterally by 44 visual degrees seen from the subject's location. Speakers were hidden behind a projection screen and each loudspeaker was equipped with a 7.6 cm-diameter single-cone (see Figure 1).

The centers of the loudspeaker cones were separated by 60 cm and were located at a 34 cm height (above table level), which corresponded to half of the total height of the projector screen, to approximately match subjects' eye level. Auditory stimuli were presented in the horizontal plane and volume differences between the speakers were used to manipulate perceived sound sources. In the experiment, sound stimuli were white noise bursts that were presented at a volume of 77.0 dB. Sounds were presented at various locations within ranges around the visual cue locations, deviating in amplitude from zero to ten per cent. Auditory stimuli were presented at various locations in order to prevent subjects from solely memorizing two locations on the screen. Visual stimuli were presented with a slide projector (Acer X138WH) on a white projection screen (59.5 x 74.5 cm) that was placed 70 cm in front of the participant's head. The size of the projection was 56.3 cm x 71 cm. Eye movements were recorded with an EyeLink1000 (SR Research Ltd., Canada), calibrated with a 5-point calibration procedure, recording the left eye.

Design

The experiment contained two within-subjects factors: cue-target congruence (congruent or incongruent) and target delay (pre- or post-saccadic). Because the pre-saccadic condition was our main interest, the majority of the targets were presented pre-saccadically. Pre-saccadic targets were played in a range from 50 to 150 milliseconds after cue presentation, since the literature on exogenous visual cueing has shown that saccade latencies generally vary between 150 and 200 milliseconds (Clark, 1999; Lee & Spence, 2017). In post-saccadic trials, target presentation was not linked to a pre-set delay; instead, a saccadic eye movement was required for these targets to be presented.

Each participant completed a total amount of 400 trials, of which 360 trials (90%) had a pre- set target delay and 40 trials (10%) were post-saccadic. Of these 360 trials, each specific cue-target delay occurred four times, of which half were congruent and half were incongruent. Eventually, this resulted in two trials of every unique combination of factors for the pre-set subgroup and 20 trials within the post- saccadic subgroup. Subjects completed eight blocks of 50 trials, with the opportunity to take a short break after each block.

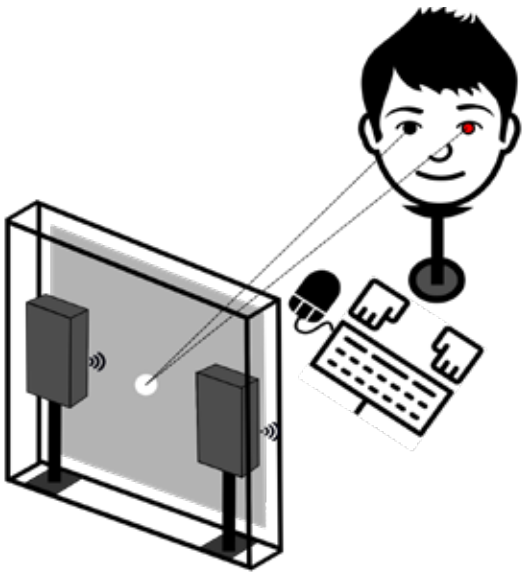

Figure 1 – Schematic illustration of the experimental set-up. *The two speakers used to manipulate sound source location are depicted as dark grey boxes. They are placed on stands to match subjects' eye level. Speakers were hidden behind the projector screen, here shown as a transparent screen. The light grey square with a white dot in the center represents the projected fixation screen. Subject's head was positioned in a custom-made chinrest and movements of the left eye were recorded. A mouse and a keyboard were used to provide and record responses*

Procedure

A mapping sequence was implemented before the actual experiment in order to be able to determine how stereo panning impacted the perceived stimulus

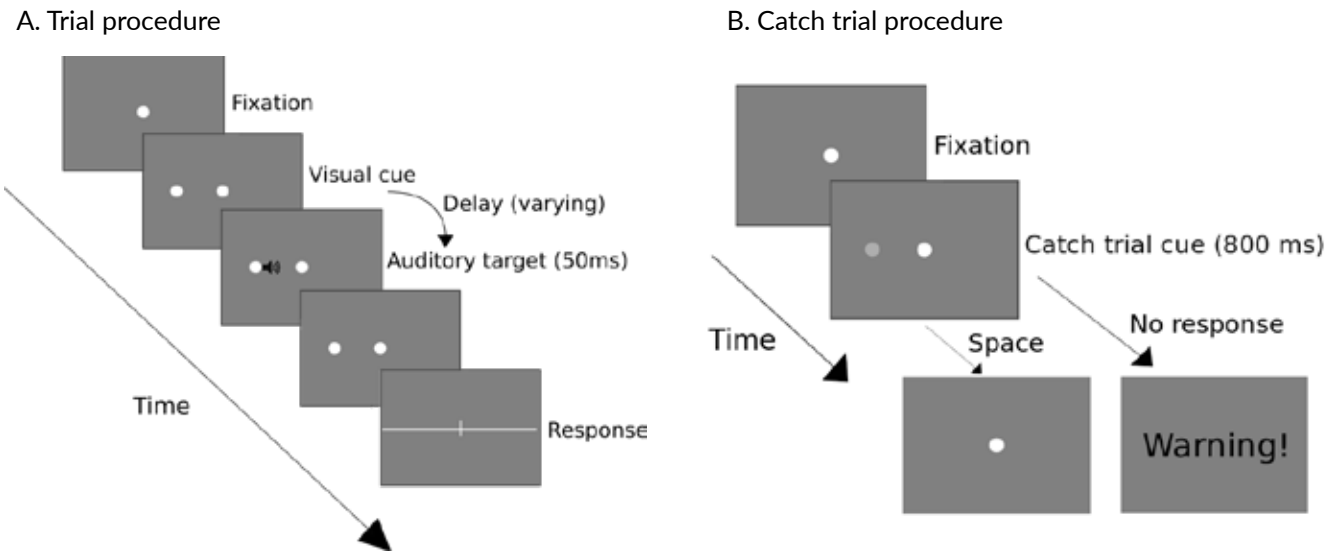

Figure 2 – Procedure. *On the left (figure A), an example of a congruent trial at the left side is depicted. On the right (figure B), the procedure of a catch trial at the left side of the screen is shown.*

location. Participants completed 168 mapping trials in total (i.e. 84 mapping trials both at the beginning and at the end of the experiment). In this mapping sequence auditory stimuli were presented over the entire horizontal plane and subjects had to indicate where they perceived sounds by clicking at the perceived location on a white horizontal line. A crosshair was shown at the clicked location and participants pressed the spacebar to confirm that location. Each subject both started and ended their participation with the mapping sequence.

After finishing the first block of mapping trials, subjects started the actual experiment (see Figure 2). First, they fixated on a white fixation dot in the middle of the screen. After 1500 milliseconds, a white dot (the visual cue/ saccade target) - identical to the fixation dot - appeared either 11° to the left or the right of the fixation point. Participants' first task was to make a saccade towards the dot as soon as it appeared on the screen. However, very shortly after presentation of the dot, an auditory target was played for 50 milliseconds either on the same side as the dot (congruent; see Figure 2A) or on the opposite side (incongruent).

Participants' second task was to localise the auditory target. Targets were presented in the horizontal plane within 2 ranges around visual cue locations in order to ensure that participants did not memorise at what locations sounds would be presented. Cue-target delay was varied in the experiment and was short enough that in the vast majority of the trials targets were presented before saccade initiation (i.e. pre-saccadically). In total, visual cues were visible for a minimum of 1550 and a maximum of 1650 milliseconds (dependent on the delay length), and responses were recorded in the same way as in the mapping trials.

To keep subjects motivated, catch trials were implemented (see Figure 2B). In these trials, visual cues were light grey instead of white and subjects were instructed to press the spacebar as soon as they perceived these dots on the screen. A warning screen with text motivating participants to pay more attention in red coloured letters followed a miss. Since colour differences between normal trials and catch trials were difficult to notice in the peripheral part of the visual field, a second purpose of catch trials was to encourage participants to make saccades. Finally, fictional accuracy scores were shown on the screen every 20 trials in order to motivate subjects to maintain focus and achieve maximal performance.

Analyses

Pre-analyses

After data acquisition, data preprocessing was carried out by using eye-tracking data to calculate saccade-target delays for each trial. Thus, for each trial we were able to determine whether target presentation actually took place before, during or after the cued saccade. Moreover, this newly calculated variable enables us to get an insight into how localisation performance responds as a function of saccade- target delay. Three subjects were excluded before analysis, since more than 50% of the eye-tracking data was missing due to technical errors. Trials from the remaining sixteen participants were accepted when: 1) cue-saccade delays were between 40 and 800 milliseconds; 2) saccade-target delays were between 600 and 600 milliseconds; 3) saccade distances were between 7° and 15° and 4) eye position at the beginning of the trial did not differ more than 3° horizontally and 1.5° vertically from fixation point, eventually leading to the rejection of 29.7% of the total number of trials (Harrison, Mattingley & Remington, 2012).

Due to technical difficulties, not all trials underwent the

same analysis. For six participants, the eye-tracker used a sampling rate of 500 Hz instead of 1000 Hz, which was the sampling rate for the remaining trials.

Statistical analyses

A mixed effect model analysis was done with localisation error value as the dependent variable, calculated by the distance between the indicated sound source and the actual source in visual degrees. Since we were not only interested in absolute localisation errors, but in the direction of these errors as well, we included signed localisation errors in our analyses, indicating whether errors were made in the direction of the visual cue (i.e. positive error values) or in the opposite direction (i.e. negative error values). The two main categorical independent variables were cue-target congruence (congruent/incongruent) and target delay (pre-/post-saccadic). Additionally, we tested for effects of delay between saccade initiation and auditory target presentation (saccade-target delay) and the distance between visual cue and auditory target (cue-target distance), which are both numeric variables. In our first model, we tested the effects of congruence and target delay on localisation performance. Our second model tested the effect of saccade-target delay on localisation performance. Saccade-target delay is a continuous variable, roughly ranging from -150 to 400 milliseconds. Finally, our third model investigated the effect of cue-target distance on localisation performance. Cue-target distance is a continuous variable, roughly ranging from 0° to 30°.

RESULTS

In our analyses we examined three ways in which the pre-saccadic shift of attention affects auditory spatial perception. Therefore, three different linear regression models were used. Results for both experiments are shown in Figure 3.

Model A tested the main outcome of interest: how target congruence affects localisation performance, (see bar graph A1, Figure 3). Here, signed errors were used as a measure for localisation performance, because this was our most informative measure. Chart A1 illustrates that under all conditions mean errors were biased towards the visual cue and that this effect is stronger for incongruent trials. This congruency effect demonstrates that errors were significantly higher for incongruent trials compared to congruent trials (Beta =-2.91, $p < 0.001$, SE = 0.12). A significant difference between pre- and post-saccadic conditions was not demonstrated.

Secondly, the way in which saccade-target delay influenced localisation performance was examined. Our second model (model B) used the unsigned error as a measure of localisation performance, testing the basic link between saccade-target delay and localisation performance. Results showed both main effects of

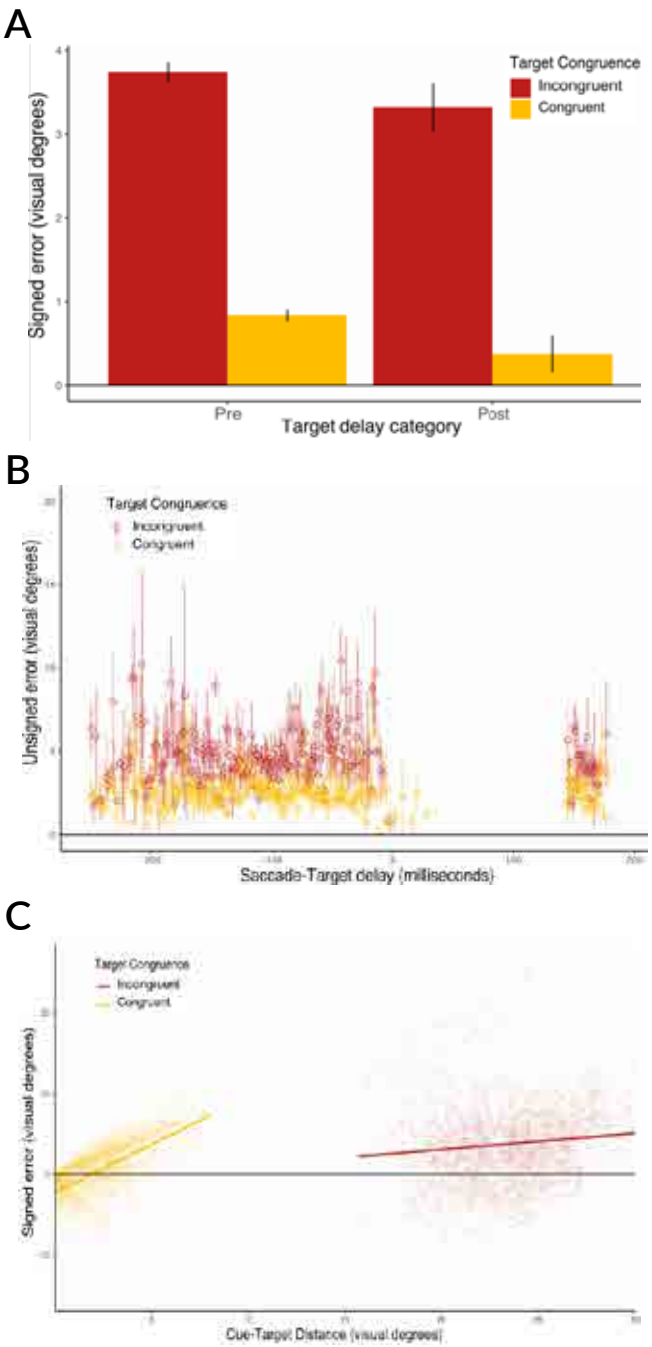

Figure 3 – The linear mixed regression models visualized. *In all three models, data of incongruent trials were shown in yellow and of congruent trials in red. Plot A demonstrates signed localisation errors (in visual degrees) per binned target delay condition. Plot B shows unsigned errors (in visual degrees) per saccade-target delay (in milliseconds). Left clusters represent trials in which targets are presented pre-saccadically and right clusters represent post-saccadic trials. Plot C shows signed errors over cue-target distance, both in visual degrees. The straight lines represent mean error values.*

target congruence (Beta = -2.12, p < 0.001, SE = 1.13 * 10-1) and saccade-target delay (Beta = -1.53 * 10-3, p < 0.01, SE = 5.78 * 10-4). The latter means that error rates decreased as saccade-target delay increased, illustrated by a subtle downwards trend over time in plot B1 (see plot B1, Figure 3).
Finally, the effect of cue-target distance on localisation performance was investigated. Similar to model A, signed error values were used as a measure of localisation performance in this model (C). A main effect of target congruence (Beta = -4.08, p < 0.01, SE = 0.70) was shown, and interestingly, an interaction between congruence and cue-target distance was demonstrated as well (Beta = 0.86, p < 0.001, SE= 0.05). This interaction means that an increase in cue-target distance resulted in a greater increase in localisation error towards visual cues for congruent trials compared to incongruent trials. This is illustrated by the difference in slopes of the red and yellow linear line in scatterplot C1 (see Figure 3).

DISCUSSION

In the first experiment, a consistent effect of target congruence was found: localisation performance in congruent trials was better compared to performance in incongruent trials. This difference was present both when absolute localisation errors were used as a measure (unsigned error), and when the direction of the error was taken into account (signed error). This congruence effect is in accordance with the results of Rorden & Driver (1999) and suggests that attracting spatial information towards the location of the upcoming target boosts localisation accuracy of this target. Furthermore, localising post-saccadically presented targets appeared to be just as difficult as localising targets that were presented before a saccade was executed.
In addition, an effect of saccade-target delay was found: sound localisation accuracy went up as auditory targets were presented later in time. This finding corresponds to our expectations, as eye location is mainly beneficial for performance when it matches the target location (Harrison et al., 2012). For pre-saccadic trials specifically, the effect demonstrates that spatial attention gradually shifts towards visual cue location from the moment of cue presentation on. Plot B1 (see Figure 3) shows that confidence intervals were minimal for trials in which targets were presented around 100 milliseconds before a saccade would be made, indicating that the pre-saccadic shift of attention most frequently occurred around 100 milliseconds before saccade execution. This is in line with studies that investigated pre-saccadic shifts in visual attention (Harrison et al., 2012).
Finally, congruency and cue-target distance interacted and showed that presenting an auditory target further away from a visual cue results in a larger decrease in sound localisation accuracy when this trial is congruent, compared to incongruent. This increase in localisation error was in the direction of the visual cue. The interaction effect might illustrate the high level of focality of spatial attention that is automatically drawn by the visual cue. Due to a combination of this focality of attention and the fact that cue-target distance is, by definition, smaller in congruent trials than in incongruent trials, increasing cue-target distance has a greater impact on congruent trials than on incongruent trials.
A factor that is known to play a role in this experiment is that – due to the short cue-target intervals – in some cases subjects experienced cues and targets as one (audiovisual stimuli), which is also known as the ventriloquist effect (Howard & Templeton, 1966; Pick, Warren & Hay, 1969). The ventriloquist effect results from vision capturing sound and influences our percepts in everyday life as well. Because the main cause of the ventriloquist effect is that visual cues appear on the screen with abrupt onset, a second experiment was conducted in which cues were presented endogenously instead of exogenously. The purpose of Experiment 2 was to equalize the weight of the ventriloquist effect in the congruent and incongruent conditions.

EXPERIMENT 2 - ENDOGENOUS CUEING

METHODS

Participants
Nineteen healthy adults (16 female, 3 male; mean age 24.8 years) who were all different from the subjects participating in Experiment 1 took part in this experiment and received twelve euros each for their participation. The experiment was stopped early for one of the subjects due to eye-tracking issues, so the eventual dataset consisted of eighteen participants (16 female, 2 male; mean age 24.9 years). All participants reported to have normal or corrected-to-normal vision and normal hearing. All subjects were naïve to the exact purpose of the experiment. The experiment took approximately 90 minutes to complete and was approved by the faculty committee of Utrecht University.

Apparatus and materials
The experimental set-up of Experiment 2 was identical to the set-up used in Experiment 1.

Design
The design of this experiment was similar, but used target delay values ranging between 100 and 200 milliseconds post-cue since latencies of endogenously cued saccades are generally greater than latencies of exogenously cued saccades (Mayfrank, Kimmig & Fischer, 1987).

Procedure
The procedure of Experiment 2 was similar to the one in Experiment 1, except for the fact that here central arrows were used as saccade cues (see Figure 3). Three white dots – of which both shape and location were

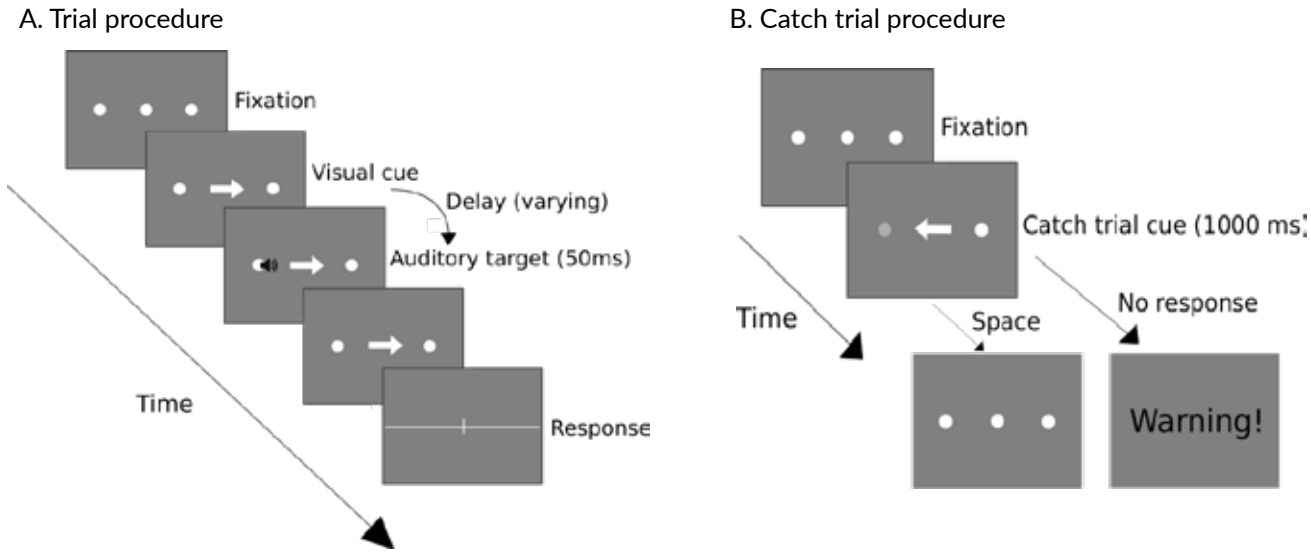

Figure 4 – Procedure. *On the left (Figure A), an example of an incongruent trial is depicted. On the right (Figure B), the procedure of a catch trial at the left side of the screen was shown.*

identical to Experiment 1 – were visible on the screen simultaneously. Subjects were instructed to fixate on the middle dot. After 1500 milliseconds, a white arrow replaced the middle dot, which could either point towards the left or the right (both at a fifty per cent chance level), indicating whether subjects should make a leftward or rightward saccade, respectively. The experiment continued the same way as Experiment 1.
In Experiment 2, catch trials were included in which white dots were visible at the same time as the grey dot appeared on the screen. In both experimental trials and catch trials, central arrows were white.

Analyses

Pre-analyses
One participant had to be excluded before analyses, due to a percentage of missing eye- t racking data above 50%. Filtering of trials was done in the same way as in experiment 1, resulting in rejection of 36,5% of the total amount of trials. For all subjects, the eye-tracker used a sampling rate of 1000 Hz.

Statistical analyses
Statistical analyses were identical to analyses in Experiment 1.

RESULTS

As depicted in bar chart A2 (see Figure 5), the strong congruency effect on performance demonstrated in Experiment 1 was less evident in Experiment 2, but still significant (Beta = -1.15, $p < 0.001$, SE = 0.10). As in Experiment 1, no main effect of target delay category was found.
Results of our second model suggest that differences between congruent and incongruent trials became less strong when the direction of localisation errors was not taken into account
(see bar chart B2, Figure 5). However, localisation errors were still significantly lower for congruent trials, compared to incongruent trials (Beta = -4.62 * 10-1, $p < 0.001$, SE = 7.68 * 10-2). The main effect of saccade-target delay, represented by the slope of the cloud of confidence intervals in plots B1 and B2, was no longer present in Experiment 2.
Finally, model C investigated how cue-target distance influenced localisation performance. Results demonstrate a similar pattern to the one shown in Experiment 1 (see plots C1 and C2, Figures 4 and 5). Both congruency (Beta = 8.67, $p < 0.001$, SE = 0.56) and cue-target distance (Beta = 0.54, $p < 0.001$, SE = 0.02) affected localisation performance. The main effect of cue-target distance demonstrates that the bias towards the visual cue increases with cue-target distance. This bias appeared to differentiate between congruency conditions, since an interaction effect was found between congruence and cue-target distance (Beta = 0.52, $p < 0.001$, SE = 0.04). The interaction showed that, also in Experiment 2, congruent trials were affected by cue-target distance to a greater extent than incongruent trials, illustrated by the difference in slopes of the red and yellow line in scatterplot C2 (see Figure 5).

DISCUSSION

As in Experiment 1, a strong effect of target congruence was demonstrated, both present when signed and unsigned errors were taken as a measure for localisation accuracy. The fact that this congruence effect remained present in this experiment indicates that saccades – at

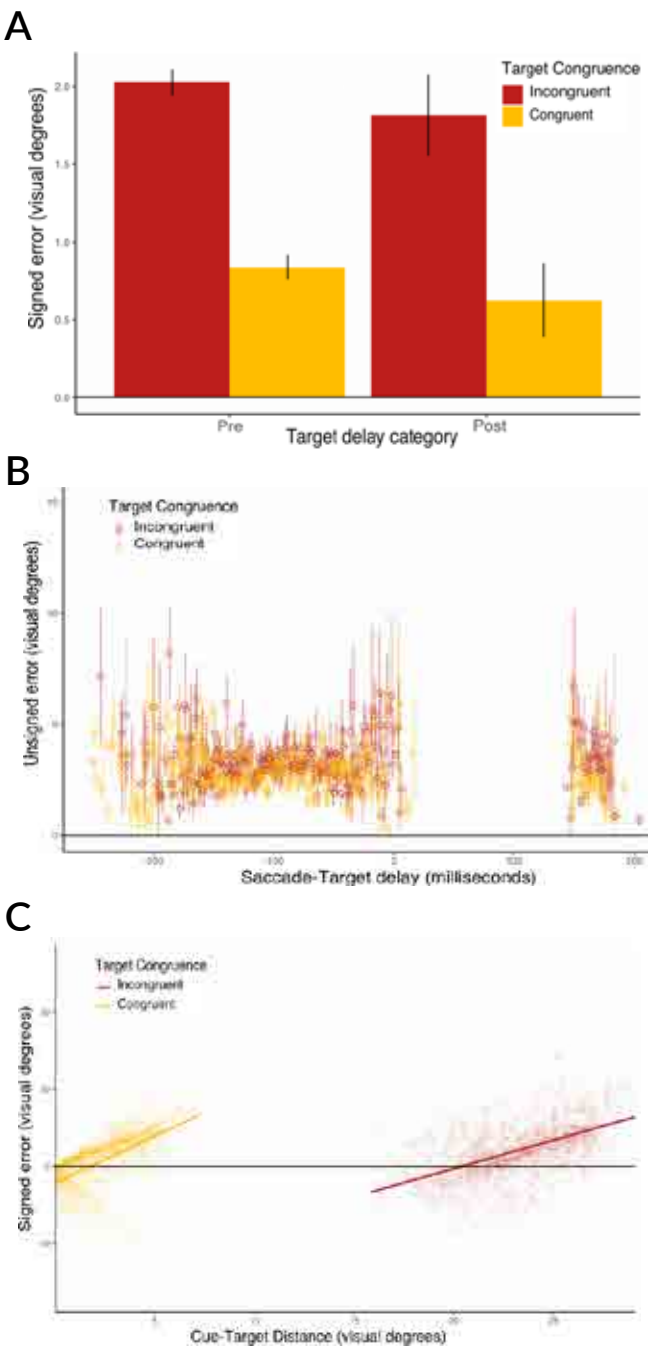

Figure 3 – The linear mixed regression models visualized. *In all three models, data of incongruent trials were shown in yellow and of congruent trials in red. Plot A demonstrates signed localisation errors (in visual degrees) per binned target delay condition. Plot B shows unsigned errors (in visual degrees) per saccade-target delay (in milliseconds). Left clusters represent trials in which targets are presented pre-saccadically and right clusters represent post-saccadic trials. Plot C shows signed errors over cue-target distance, both in visual degrees. The straight lines represent mean error values.*

least generally – affect how precise we are at localising sounds in the horizontal plane. However, as in Experiment 1, no differences in performances were found between the target delay conditions. Interestingly, when we compare plot A2 to A1 (see Figures 4 and 5), it becomes clear that localisation performance in incongruent trials was higher in Experiment 2 compared to the first experiment. For congruent trials, a clear difference was not present. This suggests that within incongruent trials, exogenous cues induce a much stronger bias towards visual cues than endogenous cues do: a pattern that is not found for trials in which cue and target occurred on the same side.

Contrary to expectations, the effect of saccade-target delay demonstrated in Experiment 1 was no longer present in Experiment 2. This means that sound localisation accuracy did not increase as targets were presented later in time. However, even though a saccade-target delay effect was not demonstrated, Experiment 2 did show minimal variation in localisation errors in trials where sounds were presented between 110 milliseconds and 80 milliseconds before saccade onset (see plot B2, Figure 5). This suggests that for endogenous saccades, pre-saccadic shifts of attention take place less consistently in time and generally closer to the moment of saccade execution, compared to exogenous saccades.

As was expected, here too it was shown that sound localisation accuracy went down (i.e. the bias towards cue location increased) as cue-target distances increased. This was demonstrated by the positive slopes of both red and yellow linear lines in plot C2 (see Figure 5). The interaction between congruency and cue-target distance was replicated in Experiment 2, which supports the earlier mentioned suggestion that shifts of attention before saccade execution tend to be quite focal. Because this interaction remained present in Experiment 2, it can be concluded that the ventriloquist effect was not the only factor driving the demonstrated bias towards visual cue location.

GENERAL DISCUSSION

The aim of our study was to examine the possible link between saccades and auditory attention following a number of studies, which have demonstrated that visual attention shifts in the direction of an upcoming saccade just before that saccade is executed (Deubel & Schneider, 1996; Godijn & Pratt, 2002; Kowler et al., 1995). A pre-saccadic shift of auditory attention in the direction of the upcoming saccade was documented as well, but only in a speeded sound discrimination task (Rorden & Driver, 1999).

Our results provide the first evidence that auditory localisation accuracy – as one of the core characteristics of auditory perception - is affected by the intended endpoint of an upcoming saccade, with better localisation

performance in the vicinity of the saccade destination. Additionally, this study is unique as it investigates how the pre-saccadic shift of attention influences auditory spatial perception over the pre-saccadic timespan and explicitly investigates the focality of attention.

We developed a novel paradigm and tested pre-saccadic attention effects on auditory localisation accuracy in two experiments with very similar experimental procedures. The clear differences in results between the experiments illustrate that the methodological choices - in our case the type of cueing (exogenous/endogenous) - when assessing pre-saccadic shifts of attention can have major consequences. One of the advantages of the sound localisation paradigm that we used is that it allowed us to examine multiple aspects of how the pre-saccadic shift of attention may affect auditory localisation accuracy. Hence, we were able to investigate how cue-target congruency affects localisation accuracy, whether localisation accuracy increases when saccade execution gets closer in time and the focality of the attention shift towards the intended saccade destination.

Taken together, our results demonstrate that perceived sound source locations are generally biased towards the location at which a visual cue is presented just before sound presentation and that these biases are much stronger in trials in which visual cues and auditory targets are presented on different sides. Strongly associated with this finding is the observation that the benefit of attention shifting towards saccade destination appears to decrease rapidly as sounds are presented further away from visual cues. This corresponds to what has been argued by many authors: that exogenous cross-modal cueing effects are spatially-specific rather than affecting the entire hemifield in which the cue happens to have been presented to the same extent (see Driver & Spence, 1998; Lee & Spence, 2017; Schmitt et al., 2001; Spence et al., 2004).

The observed bias towards cue location is in line with the idea that spatial cues lead to enlarged spatial representations of these cue locations in the brain, with a higher perceptual sensitivity at these locations (Carrasco, 2014; Müller & Findlay, 1987). Due to this increased perceptual sensitivity at cue locations, distances between targets and cues are underestimated. This underestimation of cue-target distance might be cancelled out when targets are presented in the vicinity of the visual cue (which is the case in congruent trials), because this location in space is processed with a higher spatial resolution. Following this argumentation, larger cue-target distances lead to greater biases towards cue locations, especially when targets and cues are presented at same sides. This is in line with the demonstrated interaction between cue-target distance and target congruence, showing that congruent trials are significantly more affected by cue-target distance than incongruent trials are.

Additionally, localisation performance increased as the delay between target presentation and saccade onset decreased. This effect appeared to be present for exogenous saccades, but not for endogenous saccades. Attention shifts most frequently took place around 100 milliseconds before saccade execution for exogenous saccades. For endogenous saccades, shifts of attention occurred around the same time point, although less consistently over participants. These findings are partially in accordance with the idea that the pre-saccadic shift of attention is linked to the motoric preparation of a saccade, which develops approximately during the 200 milliseconds preceding saccade execution (Blangero et al., 2010; Harrison et al., 2012; Rizzolatti et al., 1987; Smith, Schenk & Rorden, 2012).

However, the absence of the temporal effect in Experiment 2 shows that – contrary to what previous studies have demonstrated – the observed pre-saccadic perceptual facilitation cannot be fully explained by the motoric preparation of a saccade and indicates that a combination of covert orienting of attention and an automatic motor component seems to be the most plausible underlying mechanism. The fact that endogenous saccades did not demonstrate the same pattern as exogenous saccades might be due to the fact that endogenous cues induce shifts of attention that are partly dependent on subject's internal control and motivation, whereas exogenous cues have reflexive control over attention allocation (Jonides, 1981). This may lead to weaker attention shifts in Experiment 2 in general, which could explain the absence of effects over time. Of course, a factor in which experiments generally differed was saccade latency, since subjects reacted slower in response to endogenous cues compared to exogenous cues. Choosing different cue-target delays would have therefore possibly affected the results.

In cross-modal saccade experiments, experimental choices usually have large consequences on the results. Thus, a big challenge in studying the effects of saccades on non-visual spatial perception is to ensure that saccade eccentricities are stable over trials without allowing subjects to use visual stimuli as spatial "anchors". Our studies used visual cues at fixed locations as saccade targets, enabling us to study the effects of cue -target distance on performance. However, a disadvantage of this method was that – due to the higher spatial resolution of the visual system compared to the auditory system – subjects' responses were likely to be biased towards these visuospatial anchors. A second limitation of the current study was that the percentage of excluded trials was very high (see pre-analysis sections).

This was partially due to a high percentage of signal loss during eye tracking and partially due to the fact that subjects varied in eye location during fixation and cue presentation. Saccade latencies varied between participants as well, demonstrated by some subjects' inability to respond to catch trials on time, causing a great amount of variation in the moment of saccade execution

in both experiments. Finally, the long duration and great repetitiveness may have caused fatigue, resulting in undesirable variation in performance.

In summary, it can be stated that our studies point out multiple mechanisms underlying the saccade-linked shift of attention in the auditory domain. Thus, an automatic pre-saccadic mechanism, linked to the short time range in which eye muscles are prepared for a saccade, appears to be present to improve perception at the intended saccade location. This mechanism causes perception in multiple sensory domains at the intended saccade end location to be more sensitive, thereby altering the spatial representation of this location in the brain.

Since studying the effect of the pre-saccadic shift of attention on auditory perception is a relatively new field within attention research, there are multiple suggestions in which the current study should be followed-up. First of all, the second experiment should be replicated without using visual cues as saccade targets in order to eliminate any possible visuospatial bias in our sound localisation paradigm. Furthermore, it would be interesting for future research to focus on quantifying the saccade-programming component of the shift of attention by adding a fixation condition in which subjects are instructed to voluntarily shift attention (without executing a saccade) while measuring auditory localisation performance. This would enable us to draw conclusions about the nature of the pre-saccadic shift of attention. Finally, as has been indicated by Rorden and Driver (1999), it would also be interesting to investigate whether saccades can influence performance in touch, as well as in vision and hearing. If this appears to be true, this would imply a supra-modal shift of attention in the direction of an upcoming saccade, which would be a great step forward in the research fields of both attention and multisensory integration (Rorden & Driver, 1999).

In conclusion, our results provide the first evidence that auditory localisation accuracy is affected bythe endpoint of an upcoming saccade, with better localisation performance in the vicinity of the saccade destination. Our study might form the foundation of a completely new line of inquiry within attention research.

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REFERENCES

Blangero, A., Khan, A. Z., Salemme, R., Deubel, H., Schneider, W. X., Rode, G., . . . Pisella, L. (2010). Pre-saccadic perceptual facilitation can occur without covert orienting of attention. Cortex,46(9), 1132-1137. doi:10.1016/j.cortex.2009.06.014

Blurton, S. P., Greenlee, M. W., & Gondan, M. (2015). Cross-modal cueing in audiovisual spatial attention. Attention, Perception, & Psychophysics,77(7), 2356-2376. doi:10.3758/s13414-015-0920-7

Carrasco, M. (2011). Visual attention: The past 25 years. Vision Research,51(13), 1484-1525. doi:10.1016/j.visres.2011.04.012Clark, J. J. (1999). Spatial attention and latencies of saccadic eye movements. Vision Research,39(3), 585-602. doi:10.1016/s0042-6989(98)00190-4

Cornsweet, T. (2014). Visual Perception. Saint Louis: Elsevier Science.

Deubel, H., & Schneider, W. X. (1996). Saccade target selection and object recognition: Evidence for a common attentional mechanism. Vision Research,36(12), 1827-1837. doi:10.1016/0042-6989(95)00294-4

Driver, J., & Spence, C. (1998). Crossmodal attention. Current Opinion in Neurobiology,8(2), 245- 253. doi:10.1016/s0959-4388(98)80147-5

Farah, M. J., Wong, A. B., Monheit, M. A., & Morrow, L. A. (1989). Parietal lobe mechanisms of spatial attention: Modality-specific or supramodal? Neuropsychologia,27(4), 461-470. doi:10.1016/0028-3932(89)90051-1

Godijn, R., & Pratt, J. (2002). Endogenous saccades are preceded by shifts of visual attention: Evidence from cross-saccadic priming effects. Acta Psychologica,110(1), 83-102. doi:10.1016/s0001-6918(01)00071-3

Harrison, W. J., Mattingley, J. B., & Remington, R. W. (2012). Pre-Saccadic Shifts of Visual Attention. PLoS ONE,7(9). doi:10.1371/journal.pone.0045670

Howard I.P. & Templeton W. B. (1966). Human Spatial Orientation. Science,157(3794), 1296-1296. doi:10.1126/science.157.3794.1296

Ibbotson, M., & Krekelberg, B. (2011). Visual perception and saccadic eye movements. Current Opinion in Neurobiology,21(4), 553-558. doi:10.1016/j.conb.2011.05.012

James, W. (1910). The principles of psychology / by William James. doi:10.5962/bhl.title.47583

Jonides, J. (1981). Voluntary versus automatic control over the mind's eye's movement. In J.

B. Long & A. D. Baddeley (Eds.), Attention and performance IX (pp. 187–203). Hillsdale, NJ: Erlbaum.

Kowler, E., Anderson, E., Dosher, B., & Blaser, E. (1995). The role of attention in the programming of saccades. Vision Research,35(13), 1897-1916. doi:10.1016/0042-6989(94)00279-u

Lee, J., & Spence, C. (2017). On the spatial specificity of audiovisual crossmodal exogenous cuing effects. Acta Psychologica,177, 78-88. doi:10.1016/j.actpsy.2017.04.012

Mazer, J. A. (2011). Spatial Attention, Feature-Based Attention, and Saccades: Three Sides of One Coin? Biological Psychiatry,69(12), 1147-1152. doi:10.1016/j.biopsych.2011.03.014

Mayfrank, L., Kimmig, H., & Fischer, B. (1987). The Role Of Attention In The Preparation Of Visually Guided Saccadic Eye Movements In Man. Eye Movements from Physiology to Cognition,37-45. doi:10.1016/b978-0-444-70113-8.50008-4

Müller, H. J., & Findlay, J. M. (1987). Sensitivity and criterion effects in the spatial cuing of visual attention. Perception & Psychophysics,42(4), 383-399. doi:10.3758/bf03203097

Rizzolatti, G., Riggio, L., Dascola, I., & Umiltá, C. (1987). Reorienting attention across the horizontal and vertical meridians: Evidence in favor of a premotor theory of attention. Neuropsychologia,25(1), 31-40. doi:10.1016/0028-3932(87)90041-8

Onat, S., Libertus, K., & König, P. (2007). Integrating audiovisual information for the control of overt attention. Journal of Vision,7(10), 11. doi:10.1167/7.10.11

Pick, H. L., Warren, D. H., & Hay, J. C. (1969). Sensory conflict in judgments of spatial direction. Perception & Psychophysics,6(4), 203-205. doi:10.3758/bf03207017

Posner, M. I. (1980). Orienting of attention. Quarterly Journal of Experimental Psychology,32(1), 3-25. doi:10.1080/00335558008248231

Razavi, B., Oneill, W. E., & Paige, G. D. (2007). Auditory Spatial Perception Dynamically Realigns with Changing Eye Position. Journal of Neuroscience,27(38), 10249-10258. doi:10.1523/jneurosci.0938-07.2007

Rorden, C., & Driver, J. (1999). Does auditory attention shift in the direction of an upcoming saccade? Neuropsychologia,37(3), 357-377. doi:10.1016/s0028-3932(98)00072-4

Schmitt, M., Postma, A., & Haan, E. H. (2001). Cross-modal exogenous attention and distance effects in vision and hearing. The European Journal of Cognitive Psychology,13(3), 343-368. doi:10.1080/09541440042000089

Spence, C. J., & Driver, J. (1994). Covert spatial orienting in audition: Exogenous and endogenous mechanisms. Journal of Experimental Psychology: Human Perception and Performance,20(3), 555-574. doi:10.1037/0096-1523.20.3.555

Wahn, B., & König, P. (2015). Audition and vision share spatial attentional resources, yet attentional load does not disrupt audiovisual integration. Frontiers in Psychology,6. doi:10.3389/fpsyg.2015.01084

Sex differences in the affective and cognitive outcomes of early-life adversity research in rodents

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Early-life adversity influences brain function and behaviour and can have long-lasting consequences for humans as well as rodents. In humans, women are thought to be more sensitive to early-life adverse events and more susceptible for the development of stress-related disorders than men. In rodents however, males are thought to be more sensitive to early-life adversity than females. Although postnatal stress may be sexually dimorphic, currently most experimental procedures are designed to predict a male phenotype. The absence of female-specific paradigms impedes female research as well as our current understanding of sex differences. Therefore, we propose that researchers should develop paradigms with internal validity and adequate sensitivity to female phenotypes. This is essential for a more reliable translation of animal findings to humans and could help our understanding of stress-related disorders.

Keywords: *Early-life adversity; Behaviour; Sex differences; Rodents; Translational research*

Women are more likely than men to develop neurological and neuropsychiatric disorders, such as depression, anxiety, anorexia and multiple sclerosis (Bale & Epperson, 2015; McCarthy, 2016). Yet, rodent neuroscience research is strongly male-focussed (Beery & Zucker, 2011). Historically, an important reason for this is fluctuating ovarian hormones, which is thought to result in larger variabilities between subjects (Shansky, 2019). However, in 2014 a meta-analysis of 293 articles was performed, which concluded that females varied as much as males on a behavioural, physiological, morphological and molecular level (Prendergast et al., 2014; Shansky, 2019). Within the same year, the National Institutes of Health (NIH) started requiring researchers to study both sexes in preclinical research (Clayton & Collins, 2014). What would be the consequence of this obligation for female translational research? Are our paradigms for studying female's behavioural performance after adverse events during sensitive periods early in life (early-life adversity) currently optimal?

Despite the unequal number of studies measuring behaviour in males and females, several studies have attempted to compare the two sexes by reviewing the behavioural performance after early-life adversity in rodents. Consistently, a sex-differential effect was described, suggesting that males are more affected by early-life adversity than females (Loi et al., 2017; Walker et al., 2017). This may lead to the conclusion that rodents are not a proper model for humans. However, we propose that these rodent outcomes can be explained by the experimental protocols, which have historically been optimized for male rodents. We argue for the necessity of developing tests that are female-sensitive and have sufficient internal validity. In this article, the sex-differential outcomes of the cognitive and affective tests will be described first. Afterwards, we will explain why early-life adversity models are not developed to predict a female outcome.

OUTCOMES OF COGNITIVE TESTS

Learning and memory are complex cognitive functions negatively influenced by early-life adversity (Pechtel & Pizzagalli, 2011). Several human studies correlated childhood trauma with reduced hippocampal volume and cognitive deficits (Pechtel & Pizzagalli, 2011; Woon & Hedges, 2008; Woon et al., 2010). To causally link the behavioural effect of early-life adversity, cognitive learning and memory tasks are performed in rodents. Examples of these tasks include the object recognition task, object location task and Morris water maze. In these tests, rodents are required to remember, discriminate or localise certain objects in a stressed or non-stressed situation. These tasks are related to hippocampal function, which is particularly sensitive to environmental stressors during the postnatal period (Loi et al., 2014; Nanick et al., 2015; Oomen et al., 2009).

In studies that used learning and memory tasks, male rodents are more affected by early-life adversity than females (Bonapersona et al., 2019 Loi et al., 2017; Naninck et al., 2015; Walker et al., 2017). To elaborate, a larger percentage of studies showed an effect in males and effect sizes were larger for males compared to females (Bonapersona et al., 2019; Loi et al., 2017). Furthermore, some studies in which females did perform worse than control females, the effects did not last until adulthood (Bath et al., 2017). In line with these results, it has been argued that female rodents are less sensitive to early-life adversity. However, in control conditions without being exposed to adversity, females performed significantly worse than males on these learning and recognition tasks, which is called the 'floor' effect (Walker et al., 2017; Loi et al., 2017; Oomen et al.,

2011; Arp et al., 2016). This can explain smaller effect sizes for females compared to males. Consequently, the applied cognitive tests may not be optimal for female research and do not predict a female outcome (Bonapersona et al., 2019). Therefore, the tasks should be amended to increase female sensitivity. For example, to increase learning behaviour in females, researchers could search for objects towards which females show more interest. In addition, it has been shown that females perform better in discriminating similar objects (Bettis & Jacobs, 2012), which could be implemented in the experimental procedure. This may lead to female-specific object recognition and location tasks, which possibly overcomes the floor effect. Therefore, this could improve our approach to study female sensitivity to early-life adversity.

OUTCOMES OF AFFECTIVE TESTS

In humans, anxiety-related disorders are more prevalent in women compared to men (Bandelow & Michaelis, 2015; McCarthy, 2016; Somers et al., 2006). In rodents, anxiety-like behaviour is most commonly researched in both sexes with the main affective tests: the open field test and the elevated plus maze. In these tests, the animal chooses between two behaviours: its motivation to explore a new arena and its natural tendency to avoid open spaces (Bonapersona et al., 2019; Wigger & Neumann, 1999). In the open field test, the amount of time spent in the central part of the arena is considered a measure of anxiety. In the elevated plus maze, the proportion of time the rodent spends in the open arms of the plus-shaped arena, relative to the closed arms, is measured.

Loi et al. (2017) reported that females and males have comparable outcomes in anxiety-related paradigms, whereas Bonapersona et al. (2019) showed larger effect sizes in anxiety behaviour for males compared to females. Both these sex-differential outcomes do not correspond to the human phenotype, with women being more susceptible for anxiety-related disorders than men. It could be concluded that rodents are not a good model. However, this may be a misinterpretation, due to a female insensitivity to these anxiety-related tasks. For example, in the open field test, females naturally spend less time in the central part of the arena compared to males (Bath et al., 2017). This may explain the small effect sizes for females. Consequently, new tasks should be developed for females to research anxiety-like behaviour.

TIMING AND METHODS FOR EARLY-LIFE ADVERSITY

In humans, men are more affected by stress before and during birth, whereas women are more prone to develop affective disorders due to stress events after birth (Bale & Epperson, 2015; Bonapersona et al., 2019). The postnatal period of rodents corresponds to approximately the sixth month of pregnancy in humans regarding fetus development. Therefore, inducing stress in the postnatal period of rodents, may lead to a larger sensitivity for males compared to females. Consequently, a new model for early-life adversity exposure to females will be advisable. Since birth of humans corresponds to postnatal day 7 of mice (Dutta & Sengupta, 2016), stress induction should preferably start from postnatal day 7 in female stress paradigms.

Some early-life adversity models are based on limited maternal care. This way of inducing early-life adversity may also lead to a sex-bias, because male pups receive more attention individually and are more frequently licked and groomed by the mother (Oomen et al., 2009). It may also partly explain larger effect sizes after early-life adversity in males compared to females (Bonapersona et al., 2019). The inequality of the received level of maternal care can be overcome by the development of a female-based early-life adversity model, which does not depend on limited maternal care.

DISCUSSION

Overall, women are more susceptible for stress-related disorders than men (Bale & Epperson, 2015; Kessler et al., 2015; Steel et al., 2014). However, this does not correspond to rodent studies in which males show larger effect sizes, in all behavioural domains, compared to females after early-life adversity (Loi et al., 2017; Bonapersona et al., 2019). The most noteworthy sex differences are found in the cognitive tasks (Walker et al., 2017), while the affective tests give less striking sex-differential outcomes. The question is whether this concludes that female rodents are more resilient than males. We argue that rodent studies are not mirroring the human situation because of the timing of exposure to early-life adversity, the sex-biased amount of received maternal care and the insensitivity of female rodents to behavioural tasks. With a meta-analysis, researchers can test whether the sex-differential outcomes can be explained by variation in these factors. If these variables explain the sex-differential results, researchers could customise the experimental paradigms for existing models and the behavioural test battery. Although some changes have been suggested in this article, future studies can elaborate on the design of these models and paradigms. This is an ongoing research topic in the field of stress research. Considering adult stress models, female-specific social stress paradigms have been designed to effectively induce social stress in females (Haller et al., 1999; Harris et al., 2018; Herzog et al., 2009; Schmidt et al., 2010). Similarly, female-specific early-life adversity models could be developed. Consequently, a dichotomy between the paradigms for males and females will be necessary. This could result in a sex-directed phenotype and a comparable sensitivity for adverse early-life events in rodent males and females. Even though a sex-differential comparison will be more difficult, this will produce a more reliable translational model for female early-life adversity research.

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CONFLICT OF INTEREST

The authors declare that they do not have a conflict of interest.

REFERENCES

Arp, J. M., Ter Horst, J. P., Loi, M., den Blaauwen, J., Bangert, E., Fernández, G., ... & Krugers, H. J. (2016). Blocking glucocorticoid receptors at adolescent age prevents enhanced freezing between repeated cue-exposures after conditioned fear in adult mice raised under chronic early life stress. Neurobiology of learning and memory, 133, 30-38.

Bale, T. L., & Epperson, C. N. (2015). Sex differences and stress across the lifespan. Nature neuroscience, 18(10), 1413.

Bandelow, B., & Michaelis, S. (2015). Epidemiology of anxiety disorders in the 21st century. Dialogues in clinical neuroscience, 17(3), 327.

Bath, K. G., Nitenson, A. S., Lichtman, E., Lopez, C., Chen, W., Gallo, M., ... & Manzano-Nieves, G. (2017). Early life stress leads to developmental and sex selective effects on performance in a novel object placement task. Neurobiology of stress, 7, 57-67.

Beery, A. K., & Zucker, I. (2011). Sex bias in neuroscience and biomedical research. Neuroscience & Biobehavioral Reviews, 35(3), 565-572.

Bettis, T., & Jacobs, L. F. (2012). Sex differences in object recognition are modulated by object similarity. Behavioural brain research, 233(2), 288-292.

Bonapersona, V., Kentrop, J., Van Lissa, C. J., van der Veen, R., Joels, M., & Sarabdjitsingh, R. A. (2019). The behavioral phenotype of early life adversity: a 3-level meta-analysis of rodent studies. Neuroscience & Biobehavioral Reviews

Clayton, J. A., & Collins, F. S. (2014). Policy: NIH to balance sex in cell and animal studies. Nature, 509(7500), 282-3.

Dutta, S., & Sengupta, P. (2016). Men and mice: relating their ages. Life sciences, 152, 244-248.

Haller, J., Fuchs, E., Halász, J., & Makara, G. B. (1999). Defeat is a major stressor in males while social instability is stressful mainly in females: towards the development of a social stress model in female rats. Brain research bulletin, 50(1), 33-39.

Harris, A. Z., Atsak, P., Bretton, Z. H., Holt, E. S., Alam, R., Morton, M. P., ... & Gordon, J. A. (2018). A novel method for chronic social defeat stress in female mice. Neuropsychopharmacology, 43(6), 1276.

Herzog, C. J., Czéh, B., Corbach, S., Wuttke, W., Schulte-Herbrüggen, O., Hellweg, R., ... & Fuchs, E. (2009). Chronic social instability stress in female rats: a potential animal model for female depression. Neuroscience, 159(3), 982-992.

Kessler, R. C., Sampson, N. A., Berglund, P., Gruber, M. J., Al-Hamzawi, A., Andrade, L., ... & Gureje, O. (2015). Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys. Epidemiology and psychiatric sciences, 24(3), 210-226.

Loi, M., Koricka, S., Lucassen, P., & Joëls, M. (2014). Age-and sex-dependent effects of early life stress on hippocampal neurogenesis. Frontiers in endocrinology, 5, 13.

Loi, M., Mossink, J. C. L., Meerhoff, G. F., Den Blaauwen, J. L., Lucassen, P. J., & Joëls, M. (2017). Effects of early-life stress on cognitive function and hippocampal structure in female rodents. Neuroscience, 342, 101-119.

McCarthy, M. M. (2016). Multifaceted origins of sex differences in the brain. Phil. Trans. R. Soc. B 371: 20150106.

Naninck, E. F., Hoeijmakers, L., Kakava-Georgiadou, N., Meesters, A., Lazic, S. E., Lucassen, P. J., & Korosi, A. (2015). Chronic early life stress alters developmental and adult neurogenesis and impairs cognitive function in mice. Hippocampus, 25(3), 309-328.

Oomen, C. A., Girardi, C. E., Cahyadi, R., Verbeek, E. C., Krugers, H., Joëls, M., & Lucassen, P. J. (2009). Opposite effects of early maternal deprivation on neurogenesis in male versus female rats. PloS one, 4(1), e3675.

Oomen, C. A., Soeters, H., Audureau, N., Vermunt, L., van Hasselt, F. N., Manders, E. M., ... & Lucassen, P. J. (2011). Early maternal deprivation affects dentate gyrus structure and emotional learning in adult female rats. Psychopharmacology, 214(1), 249-260.

Pechtel, P., & Pizzagalli, D. A. (2011). Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology, 214(1), 55-70.

Prendergast, B. J., Onishi, K. G., & Zucker, I. (2014). Female mice liberated for inclusion in neuroscience and biomedical research. Neuroscience & Biobehavioral Reviews, 40, 1-5.

Schmidt, M. V., Scharf, S. H., Liebl, C., Harbich, D., Mayer, B., Holsboer, F., & Müller, M. B. (2010). A novel chronic social stress paradigm in female mice. Hormones and behavior, 57(4-5), 415-420.

Shansky, R. M. (2019). Are hormones a "female problem" for animal research? Science, 364(6443), 825-826.

Somers, J. M., Goldner, E. M., Waraich, P., & Hsu, L. (2006). Prevalence and incidence studies of anxiety disorders: a systematic review of the literature. The Canadian Journal of Psychiatry, 51(2), 100-113.

Steel, Z., Marnane, C., Iranpour, C., Chey, T., Jackson, J. W., Patel, V., & Silove, D. (2014). The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. International journal of epidemiology, 43(2), 476-493.

Walker, C. D., Bath, K. G., Joels, M., Korosi, A., Larauche, M., Lucassen, P. J., ... & Taché, Y. (2017). Chronic early life stress induced by limited bedding and nesting (LBN) material in rodents: critical considerations of methodology, outcomes and translational potential. Stress, 20(5), 421-448.

Wigger, A., & Neumann, I. D. (1999). Periodic maternal deprivation induces gender-dependent alterations in behavioral and neuroendocrine responses to emotional stress in adult rats. Physiology & behavior, 66(2), 293-302.

Woon, F. L., & Hedges, D. W. (2008). Hippocampal and amygdala volumes in children and adults with childhood maltreatment-related posttraumatic stress disorder: A meta-analysis. Hippocampus, 18(8), 729-736.

Woon, F. L., Sood, S., & Hedges, D. W. (2010). Hippocampal volume deficits associated with exposure to psychological trauma and posttraumatic stress disorder in adults: a meta-analysis. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 34(7), 1181-1188.

Sponsors of the Journal of Neuroscience & Cognition:

Magnetic resonance imaging at ultra-high field strengths reveals neural response properties

Harvey, B.M.[1]

[1]Helmholtz Institute, Department of Experimental Psychology, Utrecht University

Magnetic resonance imaging (MRI) measures responses of biological tissues to changing magnetic fields, showing the structure of the brain. Functional MRI (fMRI) extends this to show blood flow changes, resulting from neural activity, in response to changing sensory stimuli or cognitive tasks. Initially, fMRI focussed on localising brain areas activated by these stimuli and tasks. However, around 2008, it became possible to measure responses to many stimulus or task states to reveal how (not just where) individual fMRI recording sites (or voxels) respond. The neurons within a voxel typically respond similarly, allowing researchers to measure neural response properties that previously required invasive measurements. For example, it became possible to measure the receptive field of a voxel (the area of visual space it responds to) (Dumoulin & Wandell, 2008), how this is attracted by spatial attention (Klein, Harvey, & Dumoulin, 2014), neural response functions to properties like auditory pitch (Thomas et al., 2015) and visual object numbers or sizes (Figure 1, Harvey, Fracasso, Petridou, & Dumoulin, 2015; Harvey, Klein, Petridou, & Dumoulin, 2013). Unlike invasive electrode recordings, fMRI can record the whole brain simultaneously, allowing researchers to examine changes in response properties across the brain (Harvey & Dumoulin, 2011, 2017) and information sampling between brain areas (Gravel et al., 2014; Haak et al., 2012).

MRI scanners are rated by magnetic field strength: 1.5 Tesla (T) scanners are common in low-resolution clinical structural MRI; 3T scanners allow effective fMRI. Also, beginning around 2008, a new generation of 7T scanners was developed. Philips led this development in the Netherlands, leading to the world's highest density of 7T scanners. 7T allows structural MRI down to 0.2 mm^3 resolution, revealing small cerebral blood vessels in neurovascular disease. FMRI resolutions drop below 1 mm^3, allowing separation of responses from different grey matter layers carrying feedforward signals and feedback signals (Klein et al., 2018). At lower spatial resolutions, fMRI signal quality increases hugely, as does its spatial specificity. This facilitates characterisation of both neural response properties and their changes across the brain.

The Netherlands' advanced MRI community, working with Philips, is developing a new 7T scanner at UMC Utrecht that uses magnetic resonance spectroscopy (MRS) to determine the chemical content of tissues. Clinical uses of MRS include characterising neurochemical changes in psychiatric disorders and the composition of cancers for effective drug treatments. However, MRS is difficult with current 7T designs optimised for structural MRI and fMRI, and ineffective at 3T. Work is also beginning on an experimental 14T scanner in Nijmegen. Both projects are just beginning but aim to keep the Netherlands leading advanced MRI technology.

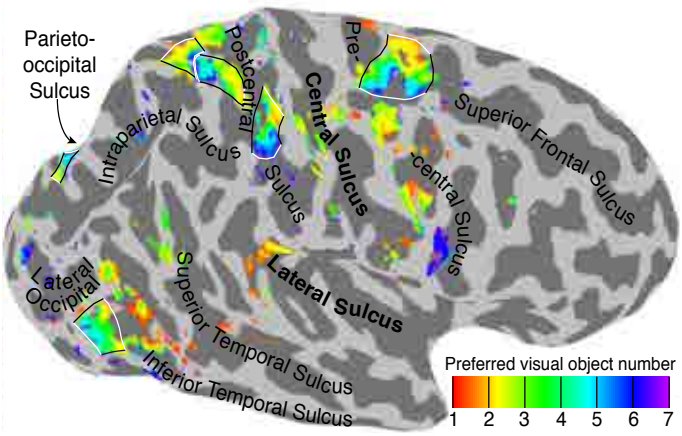

Figure 1. Response preferences for visual object number change across the cortical surface, shown using 7T fMRI. *Retrieved from Harvey, Fracasso, Petridou, & Dumoulin (2015) and Harvey, Klein, Petridou, & Dumoulin (2013).*

REFERENCES

Dumoulin, S.O., & Wandell, B.A. (2008). Population receptive field estimates in human visual cortex. Neuroimage, 39, 647-660.

Gravel, N., Harvey, B.M., Nordhjem, B., Haak, K.V., Dumoulin, S.O., Renken, R., Ćurčić-Blake, B., & Cornelissen, F.W. (2014). Cortical connective field estimates from resting state fMRI activity. Frontiers in neuroscience, 8, 339.

Haak, K.V., Winawer, J., Harvey, B.M., Renken, R., Dumoulin, S.O., Wandell, B.A., & Cornelissen, F.W. (2012). Connective field modeling. Neuroimage, 66C, 376-384.

Harvey, B.M., & Dumoulin, S.O. (2011). The relationship between cortical magnification factor and population receptive field size in human visual cortex: constancies in cortical architecture. J Neurosci 31, 13604-13612.

Harvey, B.M., & Dumoulin, S.O. (2017). A network of topographic numerosity maps in human association cortex. Nature Human Behaviour, 1, 0036.

Harvey, B.M., Fracasso, A., Petridou, N., & Dumoulin, S.O. (2015). Topographic representation-sof object size and relationships with numerosity reveal generalized quantity processing in human parietal cortex. Proc Natl Acad Sci U S A 112, 13525-13530.

Harvey, B.M., Klein, B.P., Petridou, N., & Dumoulin, S.O. (2013). Topographic representation of numerosity in the human parietal cortex. Science, 341, 1123-1126.

Klein, B.P., Fracasso, A., van Dijk, J.A., Paffen, C.L.E., Te Pas, S.F., & Dumoulin, S.O. (2018). Cortical depth dependent population receptive field attraction by spatial attention in human V1. Neuroimage, 176, 301-312.

Klein, B.P., Harvey, B.M., & Dumoulin, S.O. (2014). Attraction of position preference by spatial attention throughout human visual cortex. Neuron, 84, 227-237.

Thomas, J.M., Huber, E., Stecker, G.C., Boynton, G.M., Saenz, M., & Fine, I. (2015). Population receptive field estimates of human auditory cortex. Neuroimage, 105, 428-439.

PhD Experience

Katherine Tan

When I graduated from Medical school, my first job was as a clinician at the neurosurgery department of the UMC Utrecht. For ten months, I worked as a fresh doctor in the department with a lot of very ill people and I learned a lot about patient care and neurosurgery. It became apparent, that when I wanted to apply for the residency program, I had to enroll in a PhD position. For medical doctors, it is quite common to enroll in a PhD project concerning analyses from a database and at the same time managing a clinical trial. So, I was surprised and excited at the same time when Pierre Robe (the head of the neurosurgery department) asked me to enroll in a PhD project in the laboratory of Elly Hol. As a medical doctor, it was quite a change to start a scientific career in a laboratory. As a clinician (for me a resident not in training), many tasks concerning patients could not wait for one or two days, and every day a lot of unexpected things happened. But, as a PhD student, I suddenly could plan my whole week and I could change tasks per day. The largest difference between the clinic and the laboratory is that as a resident you are in a certain way replaceable; when I end my evening or night shift, the person who takes over for me looks after the patients I took care for in the hours before. But with my PhD project, I hold sway, and in the evening or in the weekends, no one takes over, so it is a full time responsibility.

I am two years ahead now in my PhD and I enjoy it more and more as time passes. Sometimes the pressure of obtaining new results and the pressure of finishing my thesis within 3-4 years is a lot, but as new results come in, my excitement on my subject augments and this motivates me to look further. The general atmosphere in the lab is warming and everyone is very helpful. Especially in my first months, I had to learn a lot of new things regarding laboratory techniques and there was always someone who could help me figure it out.

For future PhD students, I have two advices:

The first one is to make a rough planning on your whole project in advance and on short notice to plan your days a few weeks in advance. This way you get a clear view on what is to come, which helps you to focus on your different projects.

The second one is to give yourself some space to not think about your project. Sometimes it is difficult to let go of the running experiments or the ones that are coming up. But enjoy your free time when you have it, in order to focus even more during your 'PhD time'.

Good luck!

Outbound

"As I experienced, you don't have to travel far to feel like you're on the other side of the world"

NAME
Jeanneke Spruit

HOST INSTITUTION
University Medical Center Göttingen, Germany

TOPIC
Utilizing fasudil to attenuate ROCK activity in amyotrophic lateral sclerosis

After my internship in a lab in Utrecht, I wanted to try something new. As a scientific career did not appeal to me anymore, I wanted to find an internship where I could learn more about clinical trials. Unfortunately, the major contract research organizations were not very interested in supervising the internship of a science student... When I then came to Elly's office to talk about these struggles, she helped me out: she knew a translational neuroscience lab in Germany that was just starting with a clinical trial. I contacted the lab in Göttingen, and they invited me to do my internship with them.

When I moved to Göttingen, I was very nervous. What will my internship exactly look like? Will my flat mates even like me? Is my German good enough to live here? Fortunately, my flat mates turned out to be great, and they helped me settle down and get to know the student life. Just like many bars, our flat was decorated with feminist and anti-fascist posters and stickers. I found out that this is a big part of the Göttingen identity.

My internship turned out to be the best of both worlds for me. I spent part of my time in the lab, and for a part I was assisting at the clinical trial. ROCK-ALS is a phase IIa trial to assess the safety of the drug fasudil in amyotrophic lateral sclerosis (ALS) patients. Fasudil inhibits the activity of Rho-activated kinases (ROCK), and will hopefully benefit ALS patients. In the lab I established an assay to measure ROCK activity in blood samples, which will be used in the trial. By the time I had to leave Göttingen, the first 10 patients had been included in the clinical trial. I'm very curious to see the results in about a year.

Living in Germany turned out to be very different from living in Utrecht. I honestly thought that it would just be German-speaking Holland, but it was definitely not. To start with, German people often sound like my grandma. Some examples: my 21-year-old flat mates only used cash money ('otherwise the bank knows where you spend it'), the government forbids you to dance on certain catholic holidays ('Jesus died on this day, so there's a "Tanzverbot"'), and I painfully watched some students make their first PowerPoint slideshow ('Look, you can make the arrow fly into the screen!').

Still, I think German people are great. In my experience, they are very interested in you, and I never experienced the hierarchy that I was warned about. I like that Germans value a good work life – they will always wish you a nice "Feierabend" at the end of the day. Literally translated, it is a celebratory evening, but it is used every day to cherish the past-5-o'clock-free-time. I believe this is something we should copy.

To end this writing: I can only recommend any of you to go abroad! As I experienced, you don't have to travel far to feel like you're on the other side of the world. The minor internship is a great opportunity to switch your life around for half a year. I promise that it will be worth missing Utrecht.

Outbound

"The picture of myself being lonely and spending all my time crying and watching Netflix was wrong, obviously"

NAME
Natasja Deshayes

HOST INSTITUTION
Biomedical Center, Lund University, Lund, Sweden

TOPIC
Molecular co-chaperones in α-synuclein aggregation

Last January, with a mix of fear and excitement about the half year in front of me, I left my beloved family and friends behind and exchanged the cold Netherlands for the even colder Sweden. Lund was about to be my new hometown and the Molecular Neurobiology department of the Biomedical Centre my new working environment. I have to admit, it did not take long before I fell in love with this cute small student's town. Even at the lab I quickly felt at home; the other master students were also internationals and very helpful. As my supervisor, Christian Hansen, was also the PI and thus quite busy, it was mainly them who taught me new techniques. For my internship, I analysed the effect of a CRISPR-Cas9-mediated knockout of two molecular co-chaperones on the aggregation of α-synuclein. As with so many projects, I encountered some frustrating events. Accidentally using protease K instead of a protease inhibitor during several cell lysis experiments was just one of those events. Of course, mistakes are part of research, but I realised that I was not used to so much freedom in as well as responsibility for my project. I had to plan, conduct and analyse the experiments. In the beginning I struggled with this, but in the end it made me more confident about myself and my work, and for good reason. My supervisor and I are currently writing a manuscript for a publication of my six-month project.

In addition to working abroad, there was the experience of living abroad, which I was most insecure about. As I was living in a studio apartment and not participating in any courses at the university, I lacked both roommates and fellow students. However, the picture of myself being lonely and spending all my time crying and watching Netflix was wrong, obviously. Almost half of Lund's residents are students, which means that there are a lot of activities. In the second week, I decided to get out of my comfort zone and attend a speed friending event. Here, I noticed that almost everyone feels new and is eager to make new friends. Before I knew it, I became friends with some girls, who from then onwards were not only my dates for dinners, but also my party partners and travel buddies to Stockholm, Gothenburg and cities in Skåne. Besides all the fun events, including hiking and railbiking through Swedish nature, swimming in a quarry, dancing around the maypole during Midsommar and a lot of fika (a typical coffee and cake break), I learned more about myself. The fact that all the stuff I needed (which is not that much actually!) was in one place only, gave me peace. Even though I had some moments of being homesick, I found out that I can also be fine on my own. In absence of my regular weekly activities (sports, side job, etc.), I had much more leisure time. I started reading again, baked more often and cooked almost every day. But above all, I was astonished by how easily I got used to live in a different setting in a different country. It felt like it had been like that way longer. So, if you have the opportunity, I strongly suggest you to grab it before you regret it!

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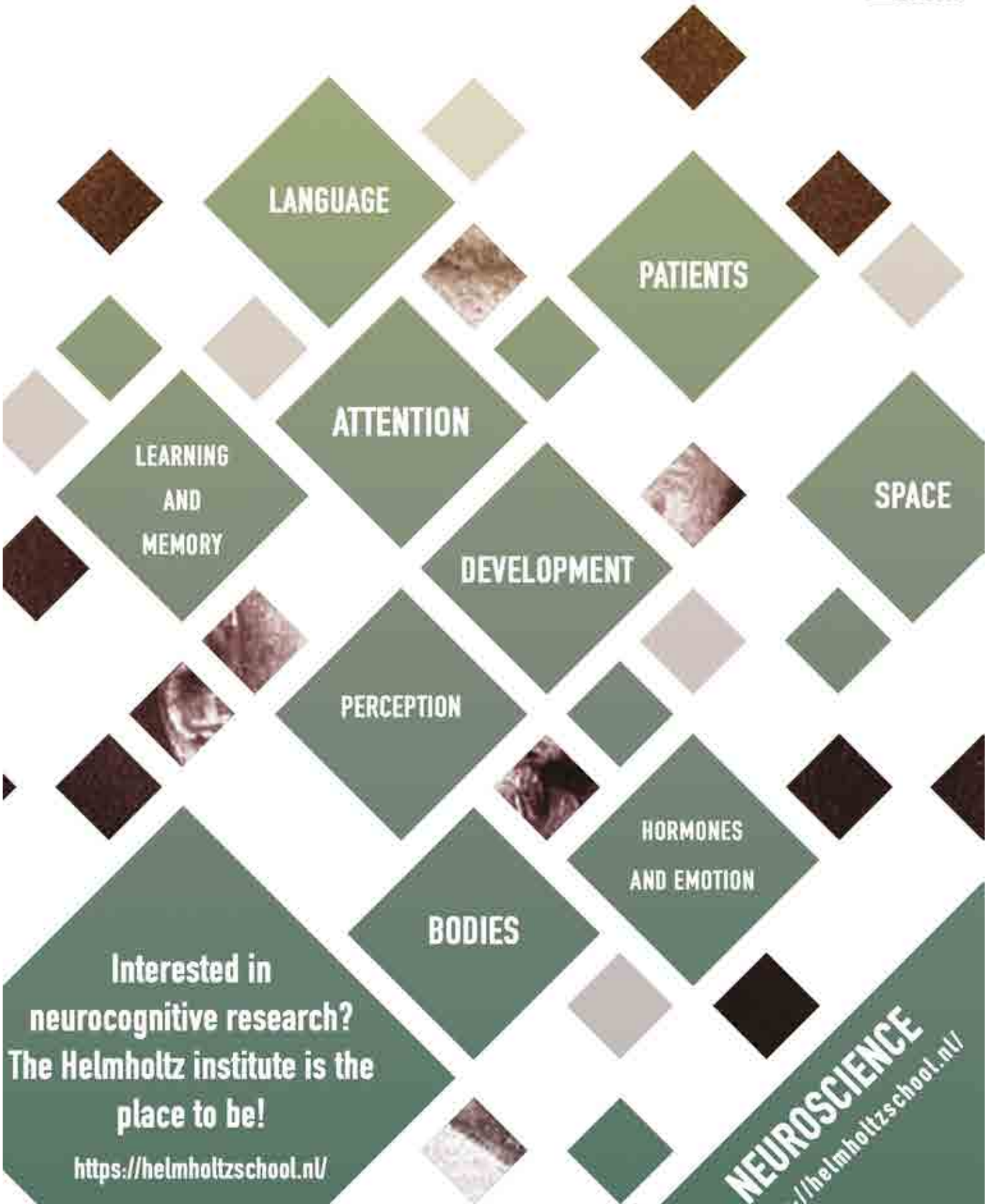

Helmholtz Lectures 2019-2020

Time: 16:00 - 17:00

Followed by drinks at Experimental Psychology
(Langeveld Building, Heidelberglaan 1, room H0.10)

30 August 2019 - **Michael Frank**
Brown University, USA
Cortical-striatal functioning: modeling and empirical perspectives
Location: Booth hall (Library)

4 October 2019 - **Siri Leknes**
Department of Psychology, University of Olso, Norway
How the brain creates hedonic experience: lessons from opioid drug studies
Location: Ruppert Red (Rood)

21 November 2019 (Thursday) - **Karen Adolph**
Department of Psychology, New York University, USA
Learning to move and moving to learn
Location: Ruppert Purple (Paars)

6 December 2019 - **David Alais**
School of Psychology, University of Sydney, Australia
TBD
Location: Ruppert Red (Rood)

31 January 2020 - **Antti Oulasvirta**
School of Electrical Engineering, University of Aalto, Finland
Psychology as the science of design: what psychological theories do
Location: TBD

Helmholtz Instituut

NCUtrecht

Interdisciplinary**views**

We have interviewed five leading experts in different fields of neuroscience about their views on interdisciplinarity in neuroscience research and healthcare. We asked them how their area of expertise can contribute to neuroscience research. And, specifically, about their experiences with interdisciplinarity within neuroscience and what they think could be improved.

Guus van Loon, MSc

During my Neurobiology Masters at the University of Amsterdam I shifted slowly from fundamental neuroscience research to studying the consumer brain and related behaviours. Currently I am a senior researcher at Bloakes. Bloakes is a market research company that uses research methods from neuroscience and psychology to answer clients' marketing questions.
Although companies like Bloakes do not always have the time and capacity to dive into fundamental research questions as deeply as the scientists at the university do, there are certainly ways to contribute to the field of neuroscience. Firstly, applied researchers stumble upon completely different and more various questions because they work in a more diverse and interdisciplinary setting. So, there seems to be a role for applied researchers to gather new questions and transfer them into academia. Secondly, in my eyes, applied researchers can make a large contribution to science by testing if established theories will sustain in a practical environment. Over the last few years, we've tested multiple theoretical concepts at Bloakes, such as the effectiveness of branded entertainment, the usage of emotions in charity campaigns and the relation between pupil dilation and cognitive load. The latter was in collaboration with experimental psychologists of Utrecht University.
Unfortunately, it is not always easy for commercial researchers to find a way into university to share newly derived knowledge. Interdisciplinary collaborations are certainly key here. Research companies can provide scientists with interesting 'real world' data and new extensive questions. Also, they often have the proper scope to increase the relevance of scientific studies. Additionally, academia may help applied researchers to attract a larger scientific audience by collective projects and publications. This way, both sides will benefit from a collaboration.

Prof. Dr. Freek Hoebeek

I am a trained biomedical scientist (University of Amsterdam) with a PhD in fundamental neuroscience (Erasmus Medical Center Rotterdam). In 2018 I have been appointed as the Chair of Translational Research of Early Life Events and head of the UMCU department for Developmental Origins of Disease. Our research teams focus on unraveling causes and consequences of adverse early life events to identify novel therapeutic strategies.
Our research teams operate at the intersection between clinical, translational and fundamental research. Often clinicians encounter anatomical, physiological or behavioral aberrations in their patient populations of which the underlying mechanisms are not yet known. It is my vision that the lack of a proper understanding of brain mechanisms in health hampers our quest for treatment options – only when one knows how the normal brain works can one recognize what needs to be fixed. I feel that this is especially true for developmental brain disorders, since it remains unclear how temporary disruptions of normal brain development affect the outcome in later stages of life.
In collaboration with the clinicians in the departments of neonatology, obstetrics, neurology and various research units united in the spear heads Brain, Child Health, Circulatory Health and Regenerative Medicine, experts like Dr.

Cora Nijboer, Dr. Titia Lely and Dr. Caroline de Theije developed several experimental models that mimic brain pathology commonly seen in children born prematurely. I believe these models are crucial for effective development of therapeutic strategies. We now use molecular, anatomical, physiological and behavioral assessments to scrutinize the mechanisms that drive normal brain development. Using these data we are able to understand at both the cellular and network level what the impact is of, for instance, diffuse white matter injury, on the maturation of neuronal systems. In collaboration with public and private partners, such as pharmaceutical companies, we now test experimental treatment options. Hereby, we support clinicians in optimizing therapeutic interventions.
The field of neuroscience is very well connected to various research disciplines, such as social sciences, (bio) electric engineering and (veterinary) medicine. In my career I collaborated with students and professionals with widely ranging backgrounds. I gained a lot of knowledge about how my work relates to, for instance, the care provided to refractory epilepsy patients, or to children diagnosed with autism spectrum. Also my students always greatly benefitted from the broad discussions about data with their peers that brought alternative interpretations – their view of what their own data meant became more complete, which greatly helped them in becoming better neuroscience students.
What can be improved is training students in a multidisciplinary environment from early on. Science is teamwork and every member of the team needs to understand what the others are good at (or not). Especially the interaction between the (bio)medical and engineering students is of importance to be able to utilize innovations necessary to provide care for the patient of tomorrow. I always experienced the discussions with my expert fellows from bioelectronics to be very insightful, but it would take quite long before we truly understood each other and were able to appreciate the added value of collaborating.

Dr. Jeroen Dudink

I studied medicine at the University of Leuven, got a PhD on "diffusion weighted MRI of the neonatal brain" at the Erasmus University, and a Master degree in Neuroscience. Now I am working as a neonatologist in Wilhelmina Children's Hospital. I am conducting research in neonatal neurology, with a focus on: advanced neonatal neuroimaging, the neonatal cerebellum and neonatal sleep. Together with Prof. dr. Freek Hoebeek I am coordinating the research theme "Developmental Disorders".
Abnormal development of the brain during fetal and early neonatal life is shown to be a major contributor to the aetiology of many neurological disorders that manifest throughout life. Besides genetic makeup, adverse intrauterine and early extrauterine environment can lead to long-term developmental disorders. Because the vulnerable brains of babies born preterm are developing in a disrupting environment (outside the safe environment of the womb) our research field is contributing to the knowledge of early origins of brain disease. For example: there is a strong link between cerebellar hemorrhages commonly seen in preterm infants and autism, with perinatal cerebellar injury carrying the greatest risk for developing autism next to having an identical twin with autism (Wang et al., 2014). Unravelling the complex relationship between cerebellar injury in the developing brain and its associated effects in prefrontal cortical organization is needed to understand these effects.
I believe interdisciplinary research between fundamental basic neuroscientists and clinical researchers (e.g. neonatologists, gynaecologists, pediatric neurologists, developmental psychologists, psychiatrists, rehabilitation specialists) is needed in order to fill the gap between fundamental knowledge and the translation into therapies that are beneficial to infants at risk for neurodevelopmental disorders.
In close collaboration with the Department for Developmental Origins of Disease (Dr. Cora Nijboer and Prof. dr. Freek Hoebeek), the neonatology department (Prof. dr. Manon Benders) has a bench-to-bedside perinatal research approach, in order to develop translational perinatal brain injury models, and effective therapies reducing and repairing the incidence and severity of brain injury caused by perinatal problems. Examples of these collaborations, which have led to clinical trials based on basic fundamental research are: stem cell treatment for neonatal hypoxic-ischemic brain injury and allopurinol treatment to protect the brains of infants with congenital heart defects.
How can we improve? I believe that we can still improve in the way we include parents and patient organisations to participate in our research. Furthermore, I believe we should invest more in advanced hospital and home neuromonitoring of infants, namely by hardware and software development.

Prof. Dr. Elly Hol

You know me as the coordinator of the experimental clinical neuroscience (ECN) track. I am a full professor in glia biology at the UMC Utrecht, and together with my research team I am studying the role of glia in brain diseases, such as stroke, dementia, and glioma.

My scientific career started in 1985 when I moved to Utrecht to study Medical Biology (now known as Biomedical Sciences). In the final 2 years, I specialized in neuroscience by doing an internship on dopamine receptors in the catfish, going abroad for 3 months to Leuven to work on the brain of the grasshopper, doing my final internship at the Rudolf Magnus Institute on neuropeptides produced in blood cells, and writing a literature thesis on the nervous system of the gut. In 1990 I started my PhD in neuroscience at the Neurology department in Utrecht, where I first learned about glia. Then I did a 2-year post-doc in a microglia lab at the Max-Planck-Institute in Munich, and after that I worked for 17 years (as a post-doc and research group leader) at the Netherlands Institute for Neuroscience in Amsterdam. Here I focused on studying Alzheimer's disease, learned how to write grant proposals, and developed my glia research line. In 2013 I came back to Utrecht. Besides my teaching and research, I am also a member of the editorial board of the journal "Glia" and chair of the scientific advisory committee of "Alzheimer Nederland".

Studying the molecular and cellular biology of glia is crucial for understanding how glia interact with neurons and by doing so contribute to brain function in health and disease. This knowledge is important as in many brain disorders, ranging from Alzheimer's disease to schizophrenia, glia have been implicated in the pathogenesis. Thus, targeting glia function is an attractive novel therapeutic strategy, which should be considered in brain disorders.

Neuroscience is an interdisciplinary field that has researchers with backgrounds ranging from molecular and cell biology to psychology. My background in fundamental neuroscience/glia biology and extensive (inter)national network of (pre)clinical research are both important for giving the best guidance and advice to the Experimental Clinical Neuroscience (ECN) students.

Prof. Dr. Sarah Durston

I am a psychologist by training, with a focus on biological psychology. I have worked in psychiatry since my first internship at the department of psychiatry in 1995, and I obtained my PhD on MRI-imaging of the brain in ADHD in 2003. I started in psychiatry in the 1990s, the Decade of the Brain. New technical developments meant we were getting higher and higher resolution images of the brain. The development of fMRI and later DTI meant we could image new aspects of biology, such as brain function and white matter integrity. This required input from many different disciplines, with biologists, psychologists, medical doctors, physicists, data scientists, mathematicians and many others working together. As such, neuroscience has always been a truly interdisciplinary field, and my area is no exception.

The feeling in the 1990s was that we would soon understand psychiatry as an entirely biological phenomenon. These technological developments taught us a lot about the brain but did not lead to a truly biological understanding of how symptoms arise. In fact, the field is now shifting to recognize that other factors are also important, including psychological and social ones (insights that have continued to be important in clinical practice). But also that ethical and philosophical considerations come into play in defining what constitutes psychiatric malfunction. It is an important development that we are making such considerations more explicit, for example in the 'labelling project' within the UU strategic theme *Dynamics of Youth*[1]. As such, new disciplines are becoming involved in psychiatry and the neuroscience of psychiatry all the time. And that is exactly as it should be.

[1]*https://www.uu.nl/en/research/dynamics-of-youth/research/interdisciplinary-themes/developmental-labels-the-good-the-bad-and-the-contested)*

Dutch Neuroscience Meeting

Lunteren, The Netherlands
June 20th & 21st, 2019

Jesca de Jager

After the successful Mind the Brain Symposium that we as master students Neuroscience and Cognition organized ourselves, we were all excited to attend the Dutch Neuroscience Meeting (DNM) the next week. As we put in hard work to design a beautiful poster, it was nice to show our masterpieces to neuroscientists from all over the world. The DNM is set up by a multi-disciplinary programme, including clinicians, postdocs and (PhD) students, giving many different talks and poster presentations. The DNM consists of a two-day programme of which I attended the second day.

"It was nice to show our masterpieces to neuroscientists from all over the world"

Early in the morning me and other master students travelled to Lunteren, a little town in the Veluwe. After the check-in we immediately went to the poster hall to mount our posters next to 90 others. At 09:00 the first of three talk sessions began, 1,5 hours each. Multiple talks were scheduled in parallel, making us choose a session that had most of our interest. So, we scattered to attend a personal self-selected programme that lasted until the lunch break. The talks that I attended were, in my opinion, of high level with interesting data from great scientists in the neuroscience field. I especially enjoyed the second session in which I chose to attend the talk titled 'Novel molecular mechanisms of glutamate receptor trafficking underlying synaptic plasticity'. I learned new insights on the molecular mechanisms of synaptic plasticity from a fundamental- and pathological point of view.

The poster session was scheduled to break up this heavy day of information flow while enjoying the delicious arranged lunch in the poster session hall. After visitors gained new energy it was our turn to present the projects we have been working on for several months. I enjoyed answering the questions from people who stopped by and were interested in my project. The day continued with the third and last parallel talk session, which was followed by some relaxing drinks. The day ended with two plenary talks. First, the Young Talent Prize awarded to Inge Holtman (Groningen) and second, Sumantra Chattarji (Bangalore, India) was given the honour to present the final keynote lecture.

All in all, the DNM was informative, inspiring and most of all gave us a sneak peek into the neuroscientific subjects of different labs from all over the world. The atmosphere was friendly and informal while we learned new insights on high-standard research.

Mind the Brain Symposium 2019

The Stressed Brain

Angelina Kancheva - Sponsoring & Logistics:

My name is Angelina and I'm doing the Experimental and Clinical track of the Neuroscience and Cognition Master's program. I wanted to be part of the Mind the Brain Symposium committee this year because I had never done anything like that before and was genuinely curious to see how much work actually goes into organizing a big event of this sort. At the same time, I thought it would be nice to get to know some of my colleagues better through that project. Organizing and hosting a symposium seemed challenging as well, which is part of what made it appealing, since I've always enjoyed taking up new activities alongside my studies. As part of the committee, I had a shared role between Sponsoring and Logistics. Funding the symposium was one of the hardest things this year. It was a long and gradual process, which involved having a lot of patience, being persuasive as to why potential sponsors should invest in our event, and dealing with negative responses. Logistics was a more creative process, which I greatly enjoyed, especially the brainstorming part: deciding where to host the symposium, what things to include in our goodie bag, how to organize the schedule of the two symposium days, etc. It required having a vision, being consistent and flexible, and communicating effectively, which also took a great deal of learning. Overall, the most rewarding part for me was to see how things were taking shape in front of our eyes and how what we had been working towards was having a life of its own in the end. The lesson that I take away is that perseverance pays off and brings joy, even when things do not always seem manageable.

Evy van Weelden - Promotion & Webmaster:

I am Evy and I had two functions in the committee: I was part of the Promotion team and I was the Webmaster. At the beginning, Tjerk (who was the other committee member doing Promotion) and I had struggles finding out "who does what, and when and how should it be done?". After a couple of weeks discussing with each other and with the chair, we luckily found our own way of doing things. That meant we went on to meet each other weekly, next to the weekly meetings we already had with the whole committee. For me, two nights per week scheduled for Mind the Brain and still trying to manage to have time for working out, doing the writing and promo for my own hobby website, seeing friends and doing bartending, was hard. Let's say... 50% of the meetings I was tired and hungry. But, the other 50% of the meetings for Mind the Brain were so rewarding, that they cancelled out all the negative feelings I had in the other half. The work outside of the meetings felt the best; that's when we put our ideas into work. That's when we made the poster and flyer designs, Instagram pictures and Facebook promotions. And that's when I got to master the website.

I've learned a lot from being in the Mind the Brain committee. I got to learn how to design flyers, posters and banners. I can still use these skills for my own website; and hopefully later on as I want to get involved with science communication in my future career. I also got an insight into my own work ethics: how I like to work, how I communicate, how I deal with my 'allergies' and 'mistakes'.

Aftermath

We are very grateful for everyone's participation and we hope visitors had a great time during our symposium. Some of the students provided feedback and we made some conclusions out of that: the free lunch was the greatest advantage of showing up from 9 to 5, and the coffee should have been handed out in the morning so people wouldn't fall asleep during the first lectures of the day! All jokes aside, most visitors seemed to enjoy the talks, poster sessions, presentations and workshops. Thank you all so much!

BEST PRESENTATION

Sanne Boing

TITLE

The impact of asymmetrical hearing loss on multisensory spatial perception: an eye-tracking study

BEST PITCH

Andre Sahakian

TITLE

Using linguistic cues to facilitate access to awareness of visual stimuli congruent to the cues – *what you hear is what you see*

BEST ABSTRACT

Tjerk Swinkels

The effect of the urge to binge on the firing behavior of neurons in the medial prefrontal cortex.

T. P. Swinkels[1,2], J.A.S. Smeets[1], C.M. Vanmeulebrouk, I.G. Wolterink-Donselaar[1] & F.J. Meye[1]

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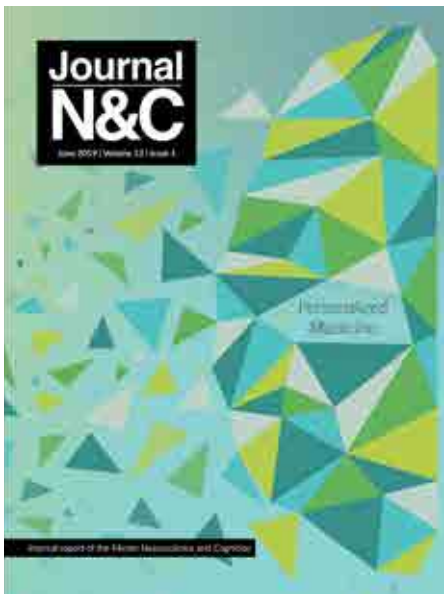
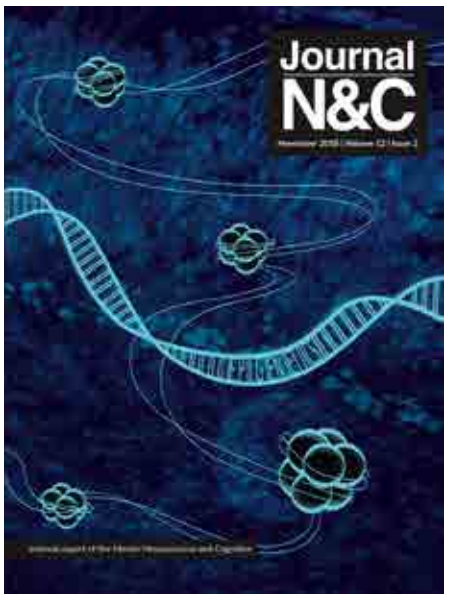
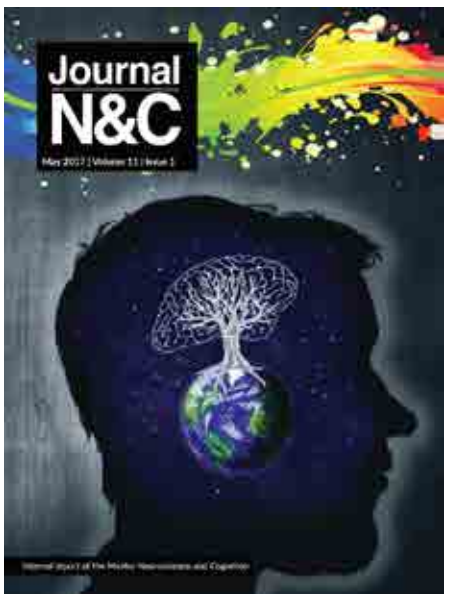
Binge eating often occurs in psychopathologies like eating disorders. Studies in humans and animal models have shown that the medial prefrontal cortex (mPFC) is heavily involved in feeding behavior and might be disrupted in binge eating. However, these studies are inconclusive, possibly due to the heterogeneity of this area, as activation of this area is shown to either increase or inhibit feeding behavior. Therefore, this research was set up to unravel how the firing behavior of neurons in the mPFC is affected by bingeing or binge-denial. The research was focused on neurons that expressed dopamine 1 receptors and projected to the Basolateral Amygdala (BLA), as this is a subpopulation of mPFC cells that is involved in eating. These cells were fluorescently labeled both genetically and via the injection of a retrograde tracer in the BLA in a mouse model. The mice were given the opportunity to binge on either tallow or chow as control in a limited access binge eating paradigm for five days. Then, current clamp electrophysiology was used to determine the firing behavior of the labeled cells. Prior to electrophysiological testing, access to the food was restricted for the mice to approximate a pre-binge configuration of the brain. Binge-denial is expected to increase the excitability of the cells, while binge eating will return the excitability to baseline levels. This research will shed light on the role of the mPFC in binge eating and may pave the road for future studies into the understanding and prevention of binge eating.

Contribute to the next issue of the journal!







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Program Manager

Of the strategic theme 'Brain'

Marjolein Sneeboer

Since I was a young girl, I was very keen on planning and scheduling my days. What will I do today, tomorrow, and next week? I liked the way I could organize and structure my life. With my studies and career it went totally different. Although I had a masterplan to become a medical doctor, sadly I was not selected to study Medicine. As an alternative, I decided to study Psychology at Leiden University: Change in career plan number 1. I enjoyed reading about the various psychiatric disorders and the available therapies. But my questions regarding the origin of these disorders and what happens in the brain were never answered. For that reason I applied to the research master Neurosciences at the VU Amsterdam, with the idea of becoming a researcher in the field of psychiatry: Change in career plan number 2. During these two years, many lectures covered behavioural and molecular aspects, such as protein analysis, RNA amplification, and animal experiments. To reassure myself that working in a laboratory was not my cup of tea, I did my first internship in the stem cell laboratory of dr. Heine. Within weeks, I was working with patient derived stem cells and became familiar with RNA isolation, western blotting, and stem cell differentiation protocols. I enjoyed it very much. Without this step outside my prefixed career plan, I would never have realized that molecular neuroscience was so fascinating and fitted me perfectly.

"Talk to people who you think are inspiring and ask about their career choices and failures"

Once again, I made a change in my career plan (number 3) and started to focus fully on a job as a molecular neuroscientist. I found a PhD position with prof. dr. Kahn (Psychiatry), prof. dr. Hol (Translational Neuroscience), and dr. de Witte (Psychiatry/Translational Neuroscience) and studied the role of the immune system in psychiatric disorders for four years. Not only did I learn about the brain's immune system (the microglia), I also boosted other skills, such as coordinating multiple research projects at the same time, dealing with failure, presenting your work in an understandable way, and creating a balance between work and personal time (your PhD does not stop after 5pm). Even though molecular research will always be in my heart, I realized that the scientific world might not be the ideal working environment for me. Furthermore, I did not see myself becoming a professor. But my qualities in organizing, planning, and connecting people and a background in research made me a very suitable candidate for multiple other jobs.

With my current job as program manager of the strategic theme 'Brain', I can use the talents that I gained throughout the years. I coordinate and think about the strategic plans that are made for all research, clinical care, and education regarding the topic 'brain'. I organize the yearly research day and assist the coordinators of the different disease areas with their activities. What I enjoy most is having close contact with researchers as well as the board of the UMC Utrecht, which makes it very dynamic. Every day is different and flexibility is needed. With the switch to program manager, I made the fourth change in my career plan and it will definitely not be my last one. There are always interesting career opportunities. As long as you know what your qualities are and what will make you happy in your work, everything is possible. So always look beyond your predefined career plan. Talk to people who you think are inspiring and ask about their career choices and failures. In my case it helped to see what more is out there. In the end I still became a doctor, only not the medical one I had in mind when I was younger.

Life Science Consulting

Empowering biomedical innovators or how to talk a lot about cool science

Teresa Calafat Pla

During the research internships in my bachelor's and master's I always asked myself the questions – Am I scientist enough for this? Am I like them? Even if I have always been interested in how the human body and the brain works, I also realized that some parts of research were boring, and I missed group work and the social component. I doubted myself several times when other lab colleagues would talk enthusiastically about a paper they had read late at night – Am I ever going to be so captivated by research? That's when I drew for myself some sort of gradient of science jobs: academic research – company research – science related job without research – no science. I told myself that I would try each next step, first translational research in academia, then research in a company, and so on, until I found my place.

My first master's internship was at Brain Center Rudolf Magnus, so for my second internship I wanted to try an R&D company. I was 9 months (and 3 more as an employee) at a medical nutrition company, looking for nutrient combinations with possible benefits for Alzheimer's disease. I was given more responsibility and also freedom to try new things. I learnt a lot about being proactive, taking charge and basically evolved from student to employee. I liked that research was applied and tangible: we wanted to make a new product out of our experiments. But I didn't like that at some point, in order to do so, I was just trying a hundred times the same thing looking for the golden nugget. I promised myself that I would make the most of being in a large company employing so many scientists, so I forced myself to talk to a lot of different colleagues and I shared my thoughts and questions. Everyone had a similar story, or knew another colleague who could guide me, etc. I asked at least a hundred times: to PhD or not to PhD?

I had many coffee appointments to chat about career pathways with people I didn't know before, and it taught me that: 1. You will only know if you like something once you try it. 2. You can always change. 3. every experience you try will be a learning experience, and never a bad decision.

I started applying for medical affairs' jobs, looking to combine scientific knowledge with general communication inside a company, but I was rejected many times because I was lacking experience and fluency in Dutch. At some point, I ended up applying for a PhD in autism models and eventually got invited to the interview with the PI, but I came across a consulting company I wasn't expecting.

I attended the UU career event and signed up for a personal conversation with the recruiters from a life science consulting firm. I wasn't sure if it was a job interview, but I prepared for one. I got invited to their offices for another interview session and got offered a job. After thinking very hard about it and taking a dozen online tests about "what job suits your personality best", I cancelled the PhD interview and accepted the offer. I have now been an associate consultant for 5 months and have discovered a field I didn't know existed: helping researchers to position themselves better to get funds or bring their innovations forward.

Ours is a young company with around 35 employees, mostly consultants but also business developers (who approach potential clients) and project managers (who follow and help throughout the project after it's granted). In the middle are the consultants, who co-write the grant application. The best thing of this job for me is that we

get to see the entire spectrum of life science research. We might help a basic science researcher apply for a starting grant to continue after a first postdoc, or we can work in a commercialization grant for a start-up with a working prototype ready to reach the market. I get to know awesome health and life science ideas and each time I need to learn and educate myself in order to co-create together with the researchers. Surprisingly, even if they are highly successful in their field, we are still useful.

"I asked at least a hundred times: to PhD or not to PhD?"

Many times, they are not aware of competitors aiming to solve the same challenge or the unique selling points of their technology. Other times, they know exactly their next experiment, but they lack the WHY? By talking a lot to them, asking many questions, challenging them and being critical, we can make them think of everything else they never thought about outside their research. For example, what are the reviewers or the investors looking for when they read your proposal? Is society asking for this innovation? Why would anyone buy the product you are designing? Why is your technology better than others doing similar innovations?

I have recently realized that I am totally out of my comfort zone, I need to learn everything, change my mindset and accept that I am not good at it yet but improving day by day. In research, I used to write in the past, about what I did in the lab and what I found out, very cautious, no big statements. Now it is the opposite: I write in the future, about the huge impact the project will have and how millions of lives could be improved. For this job you need to look at the bigger picture, be creative, brave and inspirational. Often you need to write about topics you are not an expert on, but that's no problem because the expert is the client. We bring the helicopter view, structure, and that extra twist to make it better.

Regarding the social interaction part, there's plenty of it in consulting. We work in teams of 4 or 5 and always write our projects together with a more senior colleague. We email and call often with clients and we sit together on the couch to brainstorm: – What is the real story here? What is the real pain we need to solve? Are the arguments convincing, are there any gaps?

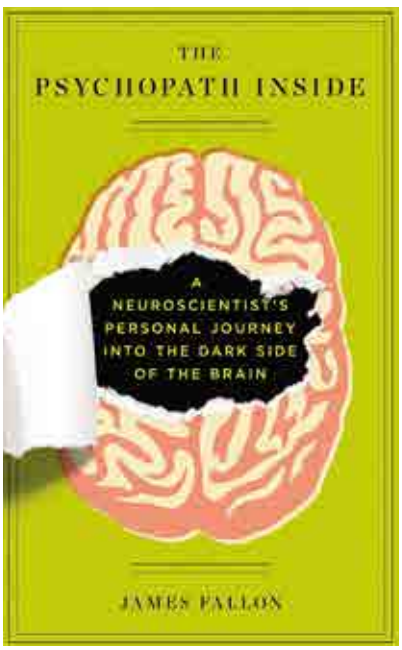
It might be that our clients still don't get the grant, but we for sure will add value by co-creating together with them and thinking outside the box to improve their ideas. If we do a good job, we might work together again, and we will hopefully see them evolve and help them along the way to bring biomedical innovations faster and smarter to the market. I don't know if this will be my job forever, but I know I am enjoying and learning a lot, and that's the most important.

The psychopath inside: A neuroscientist's personal journey into the dark side of the brain

James Fallon

Roël Vrooman

James Fallon is an American Neuroscientist. He works at the University of California, Irvine school of medicine as a professor of psychiatry. His research topics vary from adult stem cells, schizophrenia, addiction and psychopathy. For his study of psychopathy, he analysed brain images of psychopathic murderers, but as a busy man, he was working on an imaging study of Alzheimer's Disease at the same time. For this study he asked his own family to be part of the control group, in which he took part as well. When he was analysing the images of his family, which weirdly enough were blinded, but he still knew it were their images, he noticed that one of the scans matched the patterns he had previously found in the murderers. Of course, not expecting a murderer in the family, he assumed a mix up. But when checking whom the image belonged to, he found out it was his own scan. In this book, James takes you on a personal ride through his life, where he explains his theory on what psychopaths are and how they are 'made'. At the same time he correlates this theory to his own experiences, explaining what he found in his scans and family history. For his theory, which he describes as the 'Three legged stool-theory', he talks about the interaction between (1) a dysfunction in several brain regions including the orbitofrontal cortex and amygdala, (2) high risk variants of several genes and (3) early childhood trauma. Being a narrative for a large part of the book, it is quite an easy read and feels less dry than other non-fiction books. Although anecdotal evidence is not the strongest, the way in which he explains the aspects of psychopathy through his own life, does make it feel very tangible in a way numbers and figures don't. Of course his arguments and statements about psychopathy are also backed up by scientific evidence. Since psychopaths are more prevalent in society than some may expect, this book is not only a good read for anyone interested in the field of behavioural neuroscience. It is in general a good read as it can help anybody understand what a psychopath is and perhaps be more wary when they happen to meet one.



Neuroscience's Most Cited Articles

The most cited articles published since 2016
Extracted from Scopus

1 Astrocytes in physiological aging and Alzheimer's disease (2016)

Rodríguez-Arellano, J.J., Parpura, V., Zorec, R., Verkhratsky, A., Neuroscience, 323, 170-182.
Cited by 125 Documents

Astrocytes are important for homeostasis, defence and regeneration of the central nervous system. In this review, the role of astrocytes in both animal models and human tissue is elaborated, in particular the loss of function and reactivity in both physiological aging and Alzheimer's disease. These changes in astrocytes are highly heterogenous and region-specific. For example, astroglial reactivity is seen only in some regions of the brain. The review concludes that astrocytes could be a potential target for the cure of neurodegenerative diseases.

2 The serotonin system in autism spectrum disorder: From biomarker to animal models (2016)

Muller, C.L., Anacker, A.M.J., Veenstra-VanderWeele, J., Neuroscience, 321, 24-41.
Cited by 104 documents

Elevated serotonin levels in the blood, or hyperserotonemia, was the first biomarker identified in autism spectrum disorder (ASD). Serotonin has been shown to change brain and behaviour in ASD. However, its contribution to ASD pathophysiology remains unclear. This review gives a summary of the knowledge on serotonin and its role in ASD, and gives insight into the genetic background of hyperserotonemia in ASD. It also gives insight into most commonly used mouse models used for research into hyperserotonemia. It concludes with future suggestions to completely reveal the relationship between hyperserotonemia and ASD.

3 Neurobiology of fibromyalgia and chronic widespread pain (2016)

Sluka, K.A., Clauw, D.J., Neuroscience, 338, 114-129.
Cited by 91 documents

This review investigates the neurobiological mechanisms of continued pain in individuals with fibromyalgia. Fibromyalgia is a term used for chronic widespread musculoskeletal pain for which no alternative explanation can be identified. Theories suggest that fibromyalgia is linked to altered nociceptive processing in the central nervous system (CNS) and stress can augment the pain experience. Other potential mechanisms are now emerging, including the role of systemic inflammation and the peripheral nervous system involved in pain generation. This review explores the neurobiology related to the role of the CNS in nociceptive processing and evaluates studies on peripheral nervous system changes and cytokine involvement.

4 Opioid-induced hyperalgesia: Cellular and molecular mechanisms (2016)

Roeckel, L.A., Le Coz, G.M., Gavériaux-Ruff, C., Simonin, F., Neuroscience, 338, 160-182.
Cited by 88 documents

This review is about opioid-induced hyperalgesia (OIH) which is a hypersensitivity reaction induced by opioids which normally produce strong analgesia. OIH might also be associated to analgesic tolerance. Previous studies have already found some factors that modulate OIH development, such as the genetic background, sex difference of the experimental animals, and the opioid regimen. Studies also found some cellular- and molecular mechanisms underlying OIH such as activation of neuroexcitatory mechanisms, long-term potentiation, and descending pain facilitation. The intracellular and intercellular pathways involved in OIH are summarized. Lastly, this review highlights some ideas to limit OIH in the future.

5 Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review (2017)

Gentile, S., Neuroscience, 342, 154-166.
Cited by 83 documents

This systematic review highlights the prolonged and enduring effects of depression in pregnant women. The articles presented underline that antenatal depression not only affects the developing fetus, but also has effects on the newborn and the development of the child well into adolescence. Some of the effects include: irregular heart rate and hyperactivity in the brain of the fetus; altered hormone levels and electroencephalography (EEG) patterns in newborns, including depressive behaviors; externalizing and internalizing problems, and altered cortisol levels in children; and increased criminal behaviors in adolescents. The review wraps up by suggesting clinicians to be more aware of the derogatory effects of antenatal depression, despite possible adverse effects of taking antidepressants during gestation.

6 The neural basis of reversal learning: An updated perspective (2017)

Izquierdo, A., Brigman, J.L., Radke, A.K., Rudebeck, P.H., Holmen, A., Neuroscience, 345, 12-26.
Cited by 82 documents

Reversal learning is a situation in which an animal or human is trained to respond to two different stimuli under reward and punishment conditions, and thereafter is trained under reversed reward values. Reversal learning covers a set of multiple paradigms to study cognitive flexibility, and is disrupted in many psychiatric and neurological disorders. This makes reversal learning an essential paradigm in human and non-human research on the pathophysiology of these disorders. This review compares different reversal paradigms across species, provides an update on its construct validity, and reviews the major neural circuits and neurotransmitter systems that are involved.

7 Bidirectional modulation of anxiety-related and social behavior by amygdala projections to the medial prefrontal cortex (2016)

Felix-Ortiz, A.C., Burgos-Robles, A., Bhagat, N.D., Leppla, C.A., Tye, K.M., Neuroscience, 321, 197-209.
Cited by 81 documents

In this article the effects of inhibiting and activating the basolateral amygdala – medial prefrontal cortex (BLA-mPFC) pathway is investigated using optogenetics and behavioral test in mice. Activation of this pathway caused more anxious behavior on the elevated plus maze and less social interactions in the resident-intruder task and inhibition led to less anxious behavior and more social interactions. This shows the bidirectional functioning of the BLA-mPFC pathway in modulating anxious and social behaviors.

8 Influence of maternal thyroid hormones during gestation on fetal brain development (2017)

Moog, N.K., Entringer, S., Heim, C., Wadhwa, P.D., Kathmann, N., Buss, C., Neuroscience, 342, 68-100.
Cited by 78 documents

Thyroid hormones (THs) are fundamentally important for the development of the neonatal brain. The fetus is dependent on maternal THs, as its own thyroid does not produce them until mid-gestation. Therefore, it is important to determine the effects of maternal thyroid dysfunction on the development of the fetal brain. This review provides an overview of the existing literature on the effects of different forms of thyroid dysfunction, such as hypothyroxinemia or various forms of stress, on the childs' cognitive development. It also identifies knowledge gaps which need to be addressed in the future.

9 Antidepressants and gabapentinoids in neuropathic pain: Mechanistic insights (2016)

Kremer, M., Salvat, E., Muller, A., Yalcin, I., Barrot, M., Neuroscience, 338, 183-206.
Cited by 75 documents

This review elaborates on neuropathic pain, and antidepressants and gabapentinoids that are currently used for its treatment. Neuropathic pain is a chronic medical condition, caused by a lesion or disease of the somatosensory system. It is resistant to classical analgesic drugs. Noradrenaline (NA) is considered a major actor in the efficacy of antidepressants on neuropathic pain. The review gives mechanistic insights into the pathway of NA and how gabapentinoids act on NA and its receptors, in a neuropathic context.

10 Molecular neurobiology of mTOR (2017)

Switon, K., Kotulska, J., Janusz-Kaminska, A., Zmorzynska, J., Jaworski, J., Neuroscience, 341, 112-153.
Cited by 73 documents

Mammalian target of rapamycin (mTOR) is a serine-threonine kinase that controls several aspects of cell function in mammals. Its function is to check whether the intracellular condition is sufficient enough to be able to respond to extracellular stimuli. It is involved in neuronal plasticity, neuronal survival, differentiation and morphogenesis. However, the list of its known neuronal functions expands every year. This review gives an overview of the newest developments, newly identified functions and diseases associated with mTOR.

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Erratum volume 13, issue 1 – June 2019

We would hereby like to report on an erroneous printing of the abstract of the article "The role of dopamine in control over behaviour" by Mauri van den Heuvel in issue 1 of volume 13 of this journal. Please find the correct version below and disregard the previous.

With our sincerest apologies,

Editorial Board of the Journal of Neuroscience and Cognition 2018-2019

The role of dopamine in control over behaviour: The prelimbic cortex, but not striatal regions, mediates control over behaviour in rats

Van den Heuvel, M.W.[1], Verharen, J.P.[1], Vanderschuren[2], L.J.M.J. & Adan, R.A.H[1]

[1]Dept. of Translational Neuroscience, Utrecht University Medical Center, The Netherlands
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The role of ventral midbrain dopamine neurons in movement, memory, and motivation is well established, yet comparatively less is known about the role of these neurons in control over behaviour. This study aimed to investigate if and how the main output regions of ventral midbrain dopamine neurons mediate executive control over behaviour. Data was collected using behavioural-pharmacological and chemogenetic experiments. No evidence was found for the involvement of midbrain dopamine nuclei in control over behaviour; neither chemogenetic activation of dopamine neurons in the ventral tegmental area nor pharmacological blockade of dopamine receptors in the nucleus accumbens altered executive control over behaviour. Following pharmacological inactivation of the prelimbic cortex, animals exhibited impaired executive control over their behaviour. Pharmacological inactivation of the nucleus accumbens, dorsomedial striatum, or dorsolateral striatum did not affect behavioural control, but decreases in motivation were observed. These results suggest that ventral midbrain dopamine neurons do not play a role in executive control over behaviour, but the prelimbic cortex might be involved in this process via projections to the nucleus accumbens.

Keywords: *behavioural control; dopamine; striatum; accumbens; prelimbic cortex; ventral tegmental area*

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