

Asymmetric top-down modulation of ascending visual pathways in pigeons



Nadja Freund^{a,1}, Carlos E. Valencia-Alfonso^{b,1}, Janina Kirsch^c, Katja Brodmann^d,
Martina Manns^b, Onur Güntürkün^{b,*}

^a Department of Psychiatry, University of Tübingen, 72076 Tübingen, Germany

^b Biopsychology, Faculty of Psychology, Ruhr-University Bochum, 44780 Bochum, Germany

^c Fakultät für Biologie, Universität Freiburg, 79085 Freiburg, Germany

^d Center for Translational Research in Systems Neuroscience and Psychiatry, Department of Psychiatry and Psychotherapy, University Medical Center, Georg-August-University, 37075 Göttingen, Germany

ARTICLE INFO

Article history:

Received 28 February 2015

Received in revised form

9 August 2015

Accepted 13 August 2015

Available online 14 August 2015

Keywords:

Birds

Categorization

Metacontrol

Single unit recording

Thalamus

Lateralization

ABSTRACT

Cerebral asymmetries are a ubiquitous phenomenon evident in many species, incl. humans, and they display some similarities in their organization across vertebrates. In many species the left hemisphere is associated with the ability to categorize objects based on abstract or experience-based behaviors. Using the asymmetrically organized visual system of pigeons as an animal model, we show that descending forebrain pathways asymmetrically modulate visually evoked responses of single thalamic units. Activity patterns of neurons within the nucleus rotundus, the largest thalamic visual relay structure in birds, were differently modulated by left and right hemispheric descending systems. Thus, visual information ascending towards the left hemisphere was modulated by forebrain top-down systems at thalamic level, while right thalamic units were strikingly less modulated. This asymmetry of top-down control could promote experience-based processes within the left hemisphere, while biasing the right side towards stimulus-bound response patterns. In a subsequent behavioral task we tested the possible functional impact of this asymmetry. Under monocular conditions, pigeons learned to discriminate color pairs, so that each hemisphere was trained on one specific discrimination. Afterwards the animals were presented with stimuli that put the hemispheres in conflict. Response patterns on the conflicting stimuli revealed a clear dominance of the left hemisphere. Transient inactivation of left hemispheric top-down control reduced this dominance while inactivation of right hemispheric top-down control had no effect on response patterns. Functional asymmetries of descending systems that modify visual ascending pathways seem to play an important role in the superiority of the left hemisphere in experience-based visual tasks.

© 2015 Published by Elsevier Ltd.

1. Introduction

Human brains are characterized by hemispheric asymmetries that shape the operation of a large number of cognitive systems. These asymmetries are not only typical for humans but also represent a ubiquitous property of many vertebrates (Ocklenburg and Güntürkün, 2012; Vallortigara and Rogers, 2005). Most importantly, lateralized neural systems show some similarities across species and taxa, suggesting a common origin for basic components of these asymmetrically organized systems (Ocklenburg et al., 2013; Ströckens et al., 2013).

One lateralized aspect of information processing that is similar

across many species is the left hemispheric superiority in discrimination and categorization of various visual objects (Marsolek, 1999; Koivisto and Revonsuo, 2003; Laeng et al., 2003). The left hemisphere advantage in categorization was originally postulated to be a component of spatial cognition for a review see Jäger and Postma (2003). Recent studies however, made it likely that the left hemispheric superiority in categorization might go beyond space and could involve abstract-category subsystems (Andresen and Marsolek, 2005). This result pattern is supported by patient data based on imagery experiments (Palermo et al., 2008; Van der Ham et al., 2012) and found some support by imaging studies in which subjects had to apply abstract rules (Martin et al., 2008; McMamin et al., 2015; Van der Ham et al., 2009).

Animal research provides support for more general left hemisphere superiority in all kinds of tasks in which various stimuli have to be discriminated and categorized in two groups by extracting the common elements of the individual patterns. This has

* Corresponding author. Fax: +49 234 3214377.

E-mail address: onur.guentuerkuen@rub.de (O. Güntürkün).

¹ Shared first authorship.

been described in monkeys that switched to a left hemispheric categorical mode of processing after training with various stimuli (Jason et al., 1984; Vogels et al., 1994; Dépy et al., 1998). Even stronger is the support from studies with birds, where dozens of experiments in various species and with different kinds of stimuli could reveal a prominent left hemisphere superiority in categorization and various discrimination tasks (zebra finches: Alonso, 1998; chicks: Vallortigara et al., 2001; quails: Valenti et al., 2003; pigeons: Güntürkün and Kesch, 1987; Prior et al., 2004; Yamazaki et al., 2007). In some of these experiments, the animals are confronted with a large number of photographs that depict scenes with or without humans and have to discriminate between these two groups of exemplars. Finally, the birds are confronted with novel pictures and have to apply the same discrimination to these new instances. In such tasks, left hemisphere superiority is observed (Yamazaki et al., 2007). The similarity of functional lateral specialization within such a range of species provides the unprecedented possibility to search for the detailed biological mechanisms of this asymmetry in animal models.

It would, however, certainly be too farfetched to conclude from these studies that all asymmetries described above have single evolutionary background and are constituted by identical neural systems. In fact, some object classes like e.g. faces are better discriminated by the right hemisphere in humans and similar right hemispheric superiorities for the discrimination of certain objects are reported in the bird literature (Güntürkün, 1997). What animal models can offer, however, is the detailed analysis of the neurobiological constituents that prone a hemisphere to be superior in certain category tasks. Such neurobiological models can then provide searchlights for possibly similar neural solutions in the human brain. The current study was therefore undertaken to test the possibility that asymmetrically organized top-down projections in pigeons might constitute a critical neural entity for the left hemispheric superiority in discriminating and categorizing visual stimuli.

Computational, neurobiological, and imaging studies make it likely that top-down projections from higher level neural entities can modulate neural processes at earlier sensory structures where raw feature representations occur (Larkum et al., 2004; Roelfsma et al., 2002). These top-down modulations can support various subfunctions of stimulus recognition and categorization like figure-ground segregation, grouping and many more (Roelfsma et al., 2007). Even more importantly, top-down signals can serve as predictive signals in which a template is activated that predicts the expected input given the evidence derived from current bottom-up input signals (Ullman, 2007). Coutanche and Thompson-Schill (2014) could for example demonstrate that the left anterior temporal lobe of human subjects was activated before a specific object was shown and coded the retrieved object's identity. This top-down signal activated shape- and color-specific codes in relevant specialized visual areas, and thus enabled a fast recognition and categorization of visual objects. Accordingly, the dominance of the left hemisphere may arise from the influence of top-down projections, which integrate lateralized past experience into visual analysis.

To test this possibility, we conducted two experiments in the avian visual system. In the first, we recorded from single visual thalamic neurons of the nucleus rotundus (Rt) of pigeons and tested if top-down modulation from a visual telencephalic structure called "wulst" has asymmetrical effects on the left or the right thalamus. We discovered a profound asymmetry of top-down influences such that only spike patterns in the left thalamus are modified by descending systems. Thus, ascending visual projections of the left half-brain are already modulated at thalamic level by top-down telencephalic projections. This could imply that visual input into the left hemisphere is modified already at a very

early stage of analysis by past experience. Left-hemispheric top-down mechanisms may regulate attention and/or efficient stimulus analysis adapted to a categorical encoding strategy (Manns and Ströckens, 2014). As a consequence, they could select appropriate responses in conflict situations, based on an attention-based selection of stimulus components.

To test this assumption, we conducted a second study. Here, we used the metacontrol paradigm in which both hemispheres independently learn a different discrimination task. Subsequently, they are brought into conflict, such that only one of them takes charge of the behavioral output (Adam and Güntürkün, 2009; Ünver and Güntürkün, 2014). In this kind of experiment, we showed that the left hemispheric dominance in response selection (metacontrol) was abolished after transient inactivation of the left wulst. These data make it likely that the left hemispheric superiority in pigeons could at least in part be due to asymmetries of descending systems that modify ascending visual pathways due to previous learning experience.

1.1. Asymmetrical top-down control of neurons in the nucleus rotundus of pigeons

In birds, optic nerves cross completely at the optic chiasm such the input from one eye is transferred to the contralateral half brain. Ascending projections to the forebrain are processed by two parallel pathways: the tectofugal and the thalamofugal system (Fig. 1), suggested being equivalent to the extrageniculocortical and the geniculocortical visual pathways of mammals, respectively (Güntürkün, 2000). In pigeons, the tectofugal system

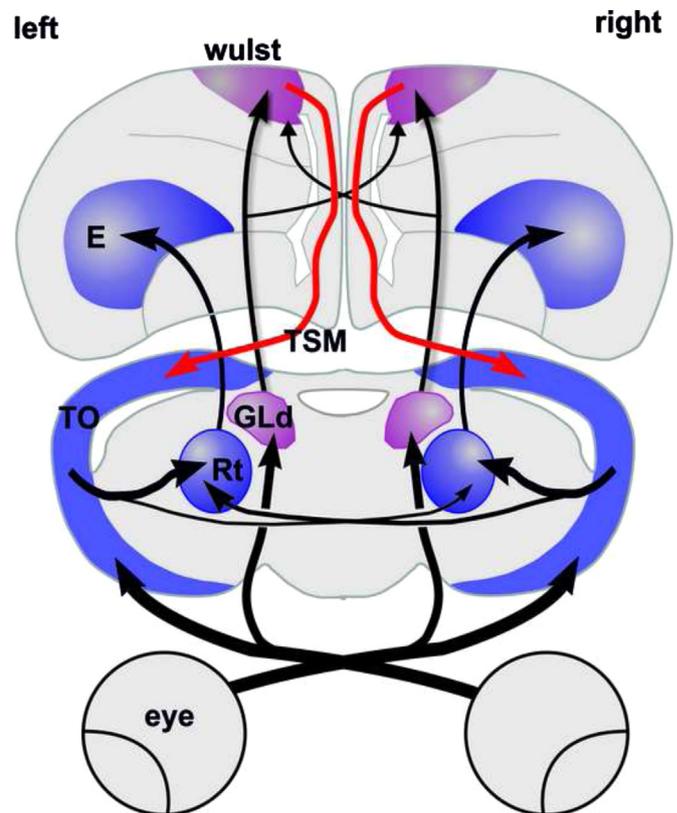


Fig. 1. Schematic depiction of the ascending and descending projections in the avian visual system. The tectofugal system (dark blue) is the most prominent pathway and ascends via the midbrain tectum opticum (TO) and the nucleus rotundus (Rt) to the entoptallium in the telencephalon. The thalamofugal system ascends via the thalamic n. geniculatus lateralis pars dorsalis (GLd) to the wulst in the telencephalon. The wulst projects via the tractus septomesencephalicus (TSM; red) to the ipsilateral tectum. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

projects from retina to contralateral midbrain tectum (TO), then bilaterally to thalamic nucleus rotundus (Rt) and finally ipsilaterally to the telencephalic entopallium (E). This pathway primarily guides visually controlled behavior in the frontal field of view (Güntürkün and Hahmann, 1999). In addition, the tectofugal system displays numerous anatomical and physiological asymmetries that correlate with lateralized visual behavior (Folta et al., 2004; Güntürkün et al., 1998; Manns and Güntürkün, 1999; Verhaal et al., 2012).

The thalamofugal system projects from retina to contralateral thalamic nucleus geniculatus lateralis pars dorsalis (GLd) and then bilaterally to the telencephalic wulst. From the wulst, a large group of forebrain fibers, the tractus septomesencephalicus (TSM), projects to the ipsilateral TO. By this top-down organization, the wulst is able to modulate ascending visual information within the tectofugal system (Manns et al., 2008).

Folta et al. (2004) could show in an electrophysiological study that single units in left and right Rt differed in some of their response properties. While Rt neurons in both half brains displayed short latency responses to contralateral flash stimulation, only left sided neurons in addition evinced a second late peak of responding. Some preliminary tests indeed could make it likely that these responses result from a top-down influence from the wulst. This could imply that only the left Rt and thus only the left sided tectofugal system is modified at a very early stage from the visual telencephalon. Therefore, we set out to analyze possible left–right differences of top-down control on the ascending tectofugal system. Using light flashes in the right and/or left entire visual field, single unit activity was recorded in the right and left Rt of anesthetized pigeons while local lidocaine injections reversibly inactivated the left or the right wulst.

1.2. Methods

13 adult homing pigeons (*Columba livia*) of undetermined sex from local breeding stocks were used for the study. All experiments were performed according to the principles regarding the care and use of animals adopted by the German Animal Welfare Law for the prevention of cruelty to animals.

Prior to the surgery the pigeons were restrained by a cloth bag and anesthetized with urethane (Sigma Deisenhofen, Germany; 25% in ad, 1 ml/100 g body weight) injected into the breast musculature divided in three doses (one every hour) to provide a prolonged and deep anesthesia. A cannula connected to a urethane syringe, was placed in the breast muscle in case additional doses were required. The anesthetized pigeons were placed on a foam couch, and mounted in a stereotaxic head holder at 90° (45° upwards relative to the pigeon atlas). The 0 point was defined by the midline of the skull (mediolateral; x) and the position of the ear bars (anterioposterior; y). Subsequently, the skull was exposed and a rectangular hole was drilled 3 mm (lateral) \times 3 mm (1.5 mm anterior and 1.5 mm posterior) relative to the 0 point in each hemisphere, and the dura mater was carefully removed. Two Hamilton syringes filled with 4% lidocaine (Sigma, St. Louis, MO) in 0.12 M phosphate buffer (pH=7.4), were inserted one into each Hyperpallium accessorium (HA), the descending out layer of the wulst (Miceli et al., 1987; Reiner and Karten, 1983) so the tip of the needle was finally located at L1.00, A13.00, and D10, according to the stereotaxic atlas of Karten and Hodos (1967). Finally, the lower eyelids were held open with medical sticky tape. Eyes were regularly moistened.

Because almost all rotundal cells respond to light flashes (Folta et al., 2004), light emitting diodes (LED) (luminance: 900 cd/m²) inserted in ocular tubes of 15 cm length and 1.5 cm diameter were used to stimulate the ipsilateral and/or contralateral eye (relative to the recorded hemisphere). The tubes were arranged in

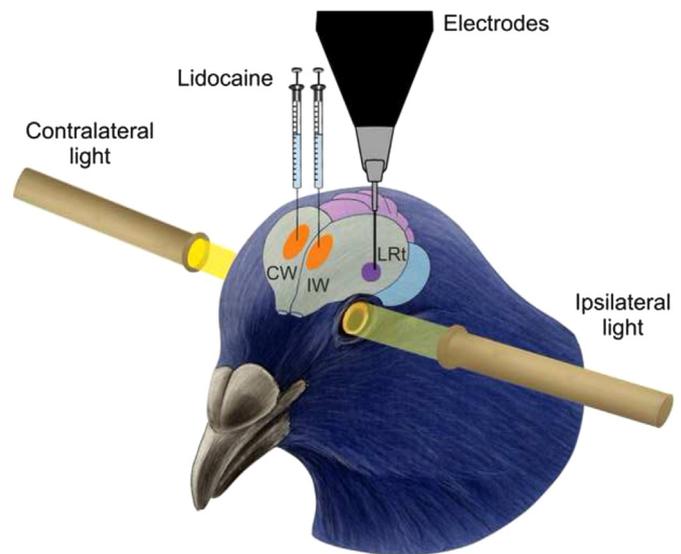


Fig. 2. Setup of experiment 1. Single cell recordings were conducted from the left or right *n. rotundus* (Rt) of an anesthetized pigeons with LED stimulations of the eyes. During recordings, activity of the ipsilateral (IW) or the contralateral wulst (CW) could be blocked with lidocaine.

an angle of 60° to the left and right from midline, corresponding to the optical axis, which guaranteed that light was transferred only to the tested eye. The background illumination was 5 lx. A trial consisted of four consecutive stimulation conditions: 1. No stimulation (NONE, baseline activity), 2. Stimulation of the ipsilateral eye (IPSI), 3. Stimulation of the contralateral eye (CONTRA), and 4. Simultaneous stimulation of both eyes (BOTH). Light flashes had a duration of 500 ms followed by 5 s interstimulus interval. Each trial was repeated 40 times. Fig. 2 shows the experimental setup.

Extracellular single-cell activity was recorded from 7 pigeons in the left Rt and from 6 pigeons in the right Rt, using a concentric arrangement of 7 glass insulated Pt/Tungsten electrodes with a shaft outer diameter of 80 μ m and metal core diameter of 25 μ m (the distance between adjacent electrodes was 305 μ m). The tips of the electrodes were sharpened and their impedance was 1–4 M Ω . The contact of the electrodes with the brain surface was marked as 0 depth, then they were advanced through the brain with a mechanical micro drive (Thomas Recording, Giessen, Germany) perpendicular to the horizontal plane, with the central electrode at $x = +3000 \mu$ m (for right Rt) or $x = -3000 \mu$ m (for left Rt) and $y: 0 \mu$ m, until a depth between 8500 μ m and 10,000 μ m was reached (the final coordinates corresponded to L3.00; A6.00, D6.5 according to Karten and Hodos (1967)). Once on each electrode a stable stimulation dependent neuronal activity within the Rt was isolated, the recording of the 40 trials started (PRE-condition). Subsequently, the ipsi- or contralateral wulst (balanced across subjects) was anesthetized with 1 μ l lidocaine from the corresponding Hamilton syringe, and the next measurement (40 trials with 4 stimulation conditions) was performed (LIDO-condition). After a recovery period of at least 30 min, the same cells were recorded again (POST-condition). Finally, the whole procedure (PRE-LIDO-POST) was repeated for the same neurons with anesthesia of the other wulst. Signals were amplified (1000 \times , SUA, Thomas Recording), filtered (BP 500–2000 Hz), monitored on oscilloscope and loudspeaker, and digitized using a custom computer software (Spike 2, CED, Cambridge) with a sampling rate of 20 kHz, 16 bit. Stimuli were digitized at a sampling rate of 1 kHz. At the end of the recording session the location of the electrodes was marked with a small electrolytic lesion by passing a 3.3–4.65 μ A AC current (50 kHz; 10 min) through the central electrode tip.

After recording, the pigeons were deeply anesthetized (0.55 ml

Equithesin/100 g body weight) and perfused intracardially with 0.9% saline followed by 4% paraformaldehyde solution in 0.1 M phosphate buffer. The brains were embedded in gelatin, cut at 40 μm in sagittal plane parallel to electrode penetrations, stained with cresylviolet, and microscopically analyzed to reconstruct recording positions.

Recordings were analyzed offline using spike sorting procedures. Peri-Stimulus-Time Histograms (PSTHs) and raster diagrams were calculated summing the spike times recorded under each stimulation condition (NONE, IPSI, CONTRA, BOTH), and anesthesia condition (PRE, LIDO, POST) for left and right wulst. PSTHs were normalized by dividing every bin value by the highest value of the session, obtaining PSTHs with discharge values between 0 and 1.

Latency was determined by calculating the lower time limit of the first of two consecutive bins above 20% of the session maximal response, while response duration was estimated by calculating the lower time limit of the first of two consecutive bins under 20% of the session maximal response, and subtracting latency to this value. Finally, response strength was determined by defining an interval according to the calculated values of response latency and response duration, for which the mean response strength was calculated between 15 ms and 115 ms after stimulus onset for contralateral and bilateral eye stimulation, and between 45 ms and 110 ms after stimulus onset for the ipsilateral stimulation.

In each pigeon, several penetrations at different stereotaxic coordinates were performed and registered into a scaled map to allow the reconstruction and verification of recording sites after the experiments. Only the recordings from electrodes localized in the nucleus Rt were analyzed. Knowing the distance of penetration of the lesion electrode, and the distances between electrodes, we measured in proportions calculated from these known values in order to avoid bias due to changes in the dimensions of the tissue through histological process. The Rt was divided in the vertical plane in medial (L2.25–3) and lateral (L3–3.75), in the horizontal plane in ventral (D4.5–5.25) and dorsal (D5.25–6), and in the frontal plane in posterior (A5.5–6.25) and anterior (A6.25–7), to allow the comparison of the neurons' distribution.

The mean activity strength, latency and duration of all responses were evaluated with ANOVA and Bonferroni posthoc tests to compare both hemispheres, and the different stimulation conditions. At the individual neuronal responses level, non-parametric Wilcoxon test was used to confirm in every single case the significant difference between the light evoked responses and the spontaneous activity obtained in the NONE-condition. This test was also used to check differences between PRE- and POST-conditions in order to verify the recovery of normal responses. Finally Wilcoxon test was also used to compare LIDO-condition with its

PRE and POST conditions to determine the influence of the lidocaine injection on rotundal activity. Only responses that showed a significant difference between PRE/POST- and LIDO-conditions were classified as wulst-modulated responses (WMRs). The frequency of WMRs was analyzed with Chi Square test, and mixed ANOVA was used to look for differences in response latency, duration, and strength between them. WMRs were analyzed separately in order to evaluate the direction and magnitude of the anesthesia influence, and the means of the responses were compared with mixed ANOVA.

1.3. Results

We recorded from 165 rotundal neurons (88 left; 77 right) that were held for several hours and were tested under repetitions of four stimulation conditions: No stimulation (NONE), stimulation of the eye ipsilateral to recorded Rt (IPSI), stimulation of the contralateral eye (CONTRA), and bilateral stimulation (BOTH). Recordings started before lidocaine was injected into the wulst (PRE), after left or right wulst lidocaine injections (LIDO) and after a recovery period (POST). Cellular activities under each condition were transformed in normalized Peri-Stimulus-Time-Histograms (PSTHs) and responses to each light stimulation showing significant activity changes during wulst anesthesia were classified as wulst modulated responses (WMRs) (see Section 1.2). As expected from the anatomical crossing of visual input, all cells responded to CONTRA and BOTH light stimulation, while 34 others responded in addition to IPSI light stimulation. These two populations (with and without ipsilateral responses) evinced a completely different pattern with respect to top-down modulation and will therefore be discussed separately.

1.3.1. Left rotundal units are modulated by left wulst

The averaged magnitude of activity changes (see Section 1.2) was compared with a mixed $2 \times 2 \times 2$ ANOVA analysis with Rt side (left/right) as between subjects factor; and light-stimulation (CONTRA, BOTH) and wulst-inactivation (ipsilateral/contralateral) as repeated measures. An overall analysis of all WMR exhibiting cells revealed that the left Rt demonstrated a significantly stronger activity reduction under wulst inactivation, compared to right Rt ($F(1,123)=8.58$; $p=0.013$). This decrease was also significantly higher for CONTRA compared to BOTH responses ($F(1,123)=9.61$; $p=0.011$) and under ipsilateral compared to contralateral wulst inactivation ($F(1,123)=6.99$; $p=0.021$). Fig. 3 shows these effects in an overall manner. The reduction of activity in the left Rt was significant for CONTRA and BOTH responses (CONTRA $p=0.000$; BOTH $p=0.000$, Bonferroni corrected) for inactivation of the

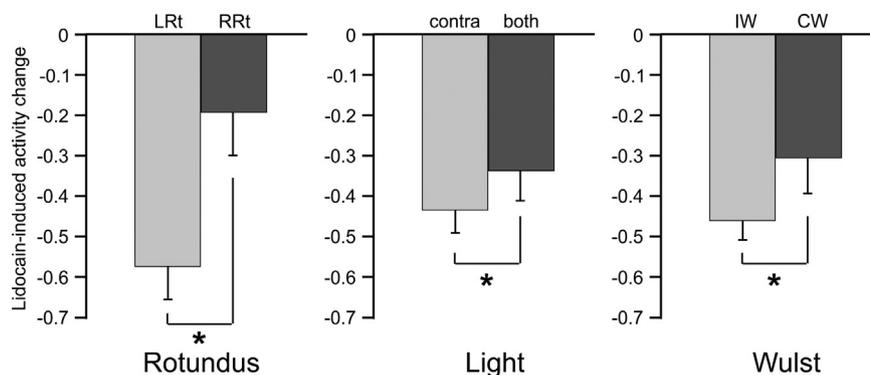


Fig. 3. Overall analysis of normalized activity changes in WMRs. To analyze the nature of wulst influence on Rt responses, normalized activity in PRE condition was subtracted from normalized activity in LIDO condition in each bin and then averaged. As a mean a value for changes in every response due to wulst anesthesia was obtained. The three main factors showed a significant impact. The activity change was larger in the left Rt (LRT) compared to right Rt (RRT). On average also lidocaine inactivation of the wulst had more impact on contralateral compared to bilateral (both) responses and were more effective in the ipsilateral (IW) compared to the contralateral wulst (CW). Bars show SE, (* $p < 0.05$).

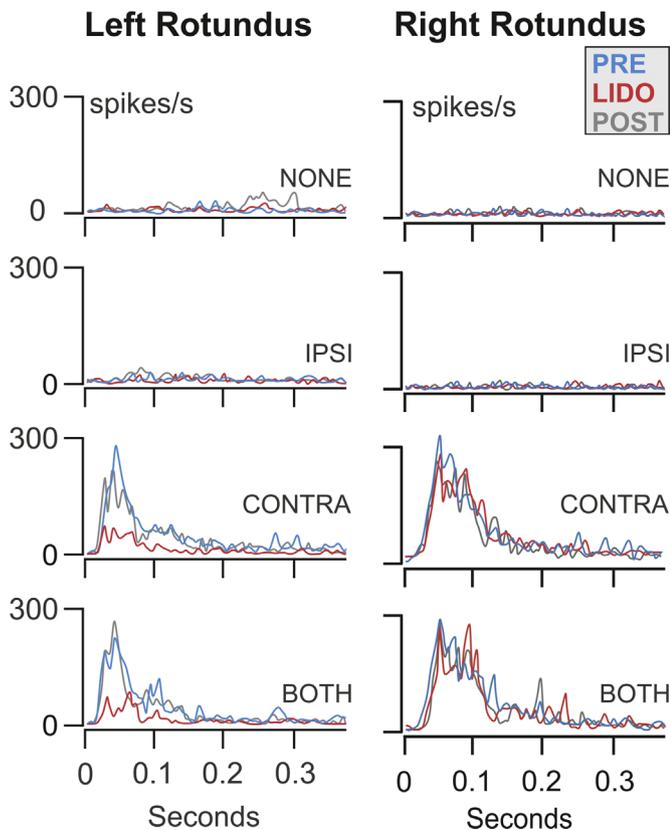


Fig. 4. Example neurons from the left and the right Rt. Spike frequencies are shown for no (NONE), ipsilateral (IPSI), contralateral (CONTRA), and bilateral visual stimulation (BOTH), before (PRE), during (LIDO) and 30 min after (POST) lidocaine infusion into the ipsilateral wulst. As visible, the left sided Rt-unit is importantly affected by lidocaine injections into the ipsilateral wulst (red trace) while no comparable effect is visible on the right side. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

ipsilateral wulst. No such effect was visible for the contralateral wulst.

Fig. 4 shows an example of cells from the left and from the right Rt. Both units did not respond to ipsilateral stimulation. The CONTRA responses of almost all (95%), and to a lesser extent the BOTH responses of these neurons were significantly modulated by wulst lidocaine injections and are therefore labeled as WMRs. Fig. 3 exemplifies that wulst anesthesia affected the visually evoked firing pattern of the left Rt-neuron profoundly while hardly modulating the right Rt-cell.

We then used one-way ANOVAs with Rt side (left/right) as a grouping factor to analyze the magnitude of activity changes for each condition: (1) CONTRA light stimulation, ipsilateral wulst inactivation; (2) BOTH light stimulation, ipsilateral wulst inactivation; (3) CONTRA light stimulation, contralateral wulst inactivation; (4) BOTH light stimulation, contralateral wulst inactivation. Only cells that showed WMRs in the analyzed condition were included.

With the whole WMRs population for each group, there was again a significant reduction in the left Rt under ipsilateral wulst inactivation (CONTRA: $F(1,105)=6.053$; $p=0.016$; BOTH: $F(1,126)=12.823$; $p=0.001$) but not under contralateral wulst anesthesia (CONTRA: $F(1,21)=3.119$; $p=0.093$; BOTH: $F(1,12)=2.081$; $p=0.175$). Fig. 5 shows the separated comparisons of left and right Rt under each stimulation and wulst conditions. These data show that there is an important asymmetry in the way each wulst influences left and right Rt. Since left wulst anesthesia reduced visually evoked activity patterns, it probably modulates left Rt-neurons in a facilitory way under normal conditions, while the right wulst has a significantly smaller effect on the right Rt.

1.3.2. No hemispheric asymmetry in the number of wulst-modulated rotundal units

Up to now only changes of strength of modulation by wulst anesthesia was reported. A difference perspective is taken, when the number of units that were significantly affected by wulst anesthesia is analyzed, irrespective of modulatory strength. In fact, the number of WMRs was not significantly different in both hemispheres ($\chi^2=1.237$; $df=1$; $N=125$; $p=0.362$). Similarly, the direction of modulation (enhanced or reduced responses) under wulst anesthesia were also equally distributed between left and right Rt ($\chi^2=1.809$; $df=1$; $N=125$; $p=0.119$). Thus, the asymmetry of top-down control only results from left-right-differences in the strength of modulation.

1.3.3. Rotundal units that are activated by the ipsilateral eye are not top-down modulated

Rotundal cells with ipsilateral responses showed several remarkable features of their own. First, none of these cells showed WMRs, independent from the stimulated eye. Thus, the wulst does not seem to modulate rotundal neurons that receive input from the ipsilateral eye system. Fig. 6a depicts an example of a session from a cell showing ipsilateral responses. As visible, blocking wulst activity with lidocaine had no effect. Neurons with ipsilateral responses were more frequent in the left Rt (23 cells; 26.44%) compared to the right Rt (11 cells; 14.29%) ($\chi^2=3.67$; $df=1$;

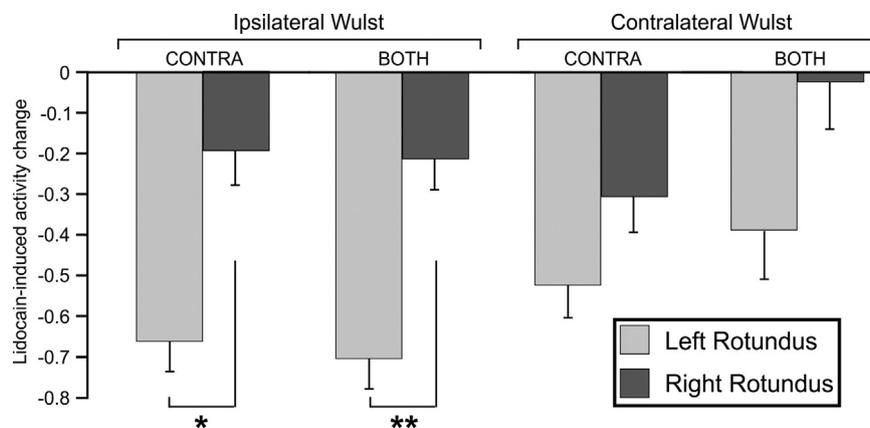


Fig. 5. Separated comparisons of asymmetric telencephalic modulation. The lateralized pattern of stronger reductions in left Rt activity as a consequence of wulst inactivation was constant over all experimental conditions. However, post-hocs analysis showed that variance was only due to changes under ipsilateral wulst anesthesia. Bars show SE, (* $p < 0.05$; ** $p < 0.01$).

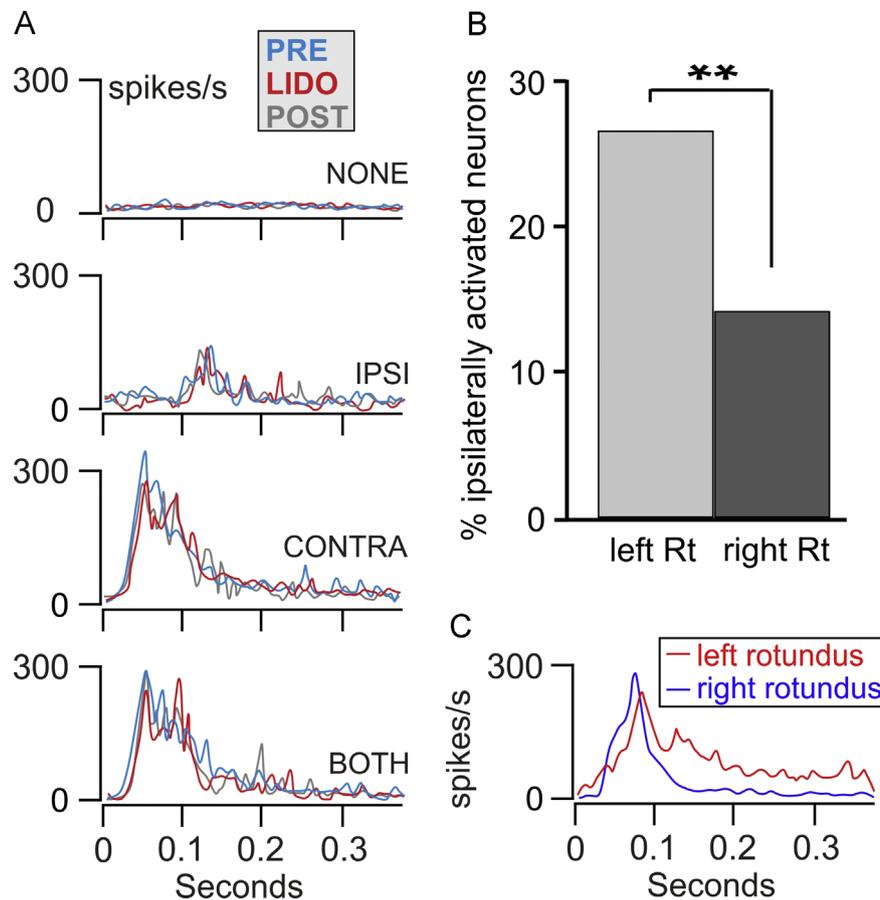


Fig. 6. Characteristics of neurons with responses to ipsilateral stimulation. (a) PSTH exemplifying the absence of changes under wulst lidocaine in each stimulation condition. (b) Percentage of neurons showing an ipsilateral response to light stimulation in the left and right Rt. (c) Different duration of ipsilateral responses in left and right Rt as exemplified in two neurons.

$N=34$; $p=0.03$) (Fig. 6b). The duration of responses to ipsilateral stimulation was longer in the left (93.1 ms; ± 5.98 SD) than in the right Rt (41.3 ms; ± 3.72 SD) (Fig. 6c) as revealed by an independent t -test comparison ($t=9.153$; $df=32$; $p < 0.01$).

Rotundal neurons with ipsilateral responses also evinced longer latencies with weaker response strengths to IPSI stimulation compared with CONTRA and BOTH responses. A 2×4 ANOVA with Rt side (left/right) as between-subjects factor and light stimulation (NONE, CONTRA, IPSI, BOTH) as repeated-measures factor revealed a significant effect of the stimulation condition factor ($F(3,495)=288.23$; $p=0.000$). Bonferroni posthoc test proved no differences between CONTRA and BOTH, but showed longer response latencies and weaker strengths of IPSI compared to CONTRA strength and BOTH (all $p \leq 0.001$) responses (Fig. 6a).

1.3.4. Responses topography and clustering

All of the analyzed recordings were obtained only from electrodes with histological confirmation of placement inside the Rt, and from brains showing an appropriate injection-induced lesion in wulst. To investigate if the localization of the cells evidenced any clustering related to the analyzed variables, the Rt was divided into 8 parts. A chi square test revealed that the recording positions were equally distributed within all Rt portions. Additionally, a mixed ANOVA showed no regional clustering concerning strength, duration and latency of neuronal responses in the 8 parts of left and right Rt. Finally, chi square analyses also revealed that the frequency of WMRs as well as the frequency of cells with ipsilateral responses showed no regional clustering or left–right asymmetry.

1.4. Discussion

Our results reveal a highly lateralized mechanism in which visually activated left rotundal neurons are strongly modulated by top-down systems of the forebrain, while activity patterns of right rotundal cells are modified to a much lower degree. In pigeons, this functional asymmetry could alter visual input to the left hemisphere by experience-based forebrain processes, while leaving right hemisphere visual input mostly unchanged. This new mechanism could enable fundamentally different modes of sensory analyses between the hemispheres. An asymmetry of attention modulation or top-down control could result in a functional framework in which the left hemisphere analyses visual patterns at a very early stage of analysis according to past experience or current goals whereas right-hemispheric visual analysis functions in a much more bottom-up way. As a result, a left hemispheric superiority in the discrimination and categorization of visual stimuli and in decision-making could result.

1.4.1. Asymmetric telencephalic modulation of the tectofugal pathway

The pigeons' tectofugal system is the major pathway for visually guided behavior. Lesions of the Rt or its telencephalic target, the entopallium, result in deficits of a large number of visual psychophysical and visuocognitive functions (Güntürkün et al., 2000). Thereby, left sided tectofugal lesions result in more severe visual discrimination deficits (Güntürkün and Hahmann, 1999). The facilitatory modulation of especially left-sided Rt-processes via descending wulst pathways are therefore able to alter visual processing in birds. Accordingly, complex visual discrimination

and categorization tasks carried out under monocular conditions are performed at a higher level using the right eye (left hemisphere) (Güntürkün, 1985; Güntürkün and Hoferichter, 1985; Von Fersen and Güntürkün, 1990; Yamazaki et al., 2007). If the asymmetry of attentional modulation or top-down control indeed modifies ascending tectofugal information processing according to past learning events that are stored in the telencephalon, we would expect that we observe no or less asymmetry in categorization tasks when the animals have no past experience with the relevant stimuli. Indeed, newly hatched chicks strongly react with their left eye seeing (right hemisphere) to sexual or agonistic stimuli that activate an inborn behavioral repertoire (Bullock and Rogers, 1992; Dharmaretnam and Rogers, 2005). Their ability to discriminate between grains and pebbles, however, requires a learning period and is, once established, more efficient with the right eye (left hemisphere). Efficient inhibition of inappropriate pecks onto pebbles thereby only depends on left-hemispheric wulst activity (Howard et al., 1980; Rogers and Anson, 1979; Rogers et al., 2007).

1.4.2. Rotundal cells with ipsilateral responses

Rt-neurons with input from the ipsilateral eye system and therewith the contralateral tectum were not under wulst control. Since all of these neurons also received input from the contralateral eye, tectofugally based bilateral integration does not seem to be modulated via forebrain systems. IPSI responses had also longer latencies compared to CONTRA and BOTH, possibly because the recrossing fibers from TO to contralateral Rt take a longer path and are unmyelinated (Saleh and Ehrlich, 1984). Comparable to a previous study (Folta et al., 2004), IPSI responses were more frequently found on the left Rt, and their durations were longer compared to right Rt. The asymmetric distribution of these cells is probably related to the fact that left Rt receives more afferents from the contralateral TO than the right Rt, enabling a more bilateral representation within the ascending left tectofugal system (Güntürkün et al., 1998). The fact that only Rt-neurons with IPSI input are devoid of a top-down forebrain control makes it likely that these neurons mediate a function were input from either eye has to reach the forebrain, irrespective of the modulations going on within the descending pathways.

It is intriguing that predominantly (only) left-hemispheric tectofugal processing is modulated by top-down mechanisms arising from the wulst. Since these mechanisms can mediate the impact of previous experiences onto visual analysis, it is likely that especially left-hemispheric processing is affected by learning. The left wulst may therefore dominate response selection in conflict tasks, which require decisions based on learning experience. This was tested in the second experiment.

2. Asymmetries of metacontrol

2.1. Introduction

Despite the fact that birds do not have a corpus callosum the hemispheres are able to transfer visual information (Catania, 1965; Letzner et al., 2014; Valencia-Alfonso et al., 2009) to interact ([Güntürkün et al., 2000, Manns and Römling, 2012]) and to also to ignore information to avoid conflicting information of both hemispheres (Palmer and Zeier, 1974). In addition, there is evidence that one hemisphere takes over control when both hemispheres are brought into conflict in pigeons ([Adam and Güntürkün, 2009, Ünver and Güntürkün, 2014]). This metacontrol has also been reported in humans (Lazarus-Mainka and Hörmann, 1978; Levy and Trevarthen, 1976; Urgesi et al., 2005), monkeys (Kavcic et al., 2000) and chickens (Vallortigara, 2000). The hemisphere

dominating (conflict) choices depends on the individual (Adam and Güntürkün, 2009), the strategy chosen (Lazarus-Mainka and Hörmann, 1978) and the design of the task (Urgesi et al., 2005). In the present study, we were interested if metacontrol in pigeons is modulated by top-down projections from the wulst and if this happens in an asymmetric manner. We trained the two eyes/hemispheres to discriminate two different color pairs. After reaching learning criterion animals were then tested with conflicting stimuli (a combination of S+ and S-) under binocular conditions. Response patterns of the animals indicated that the left hemisphere is dominating the responses. By blocking neuronal activity of the left or right wulst we were able to investigate the role of the wulst of each hemisphere on (conflict) choice behavior.

2.2. Material and methods

2.2.1. Subjects

Twenty adult pigeons (*Columba livia*) of both sexes, obtained from local breeders, were used in this experiment. Animals were kept in individual cages on a 12-h light-dark cycle. Food was restricted to keep the weight at 80% of free-feeding weight. Each bird conducted one session a day, 5 days a week. The experiments were performed in compliance with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and were approved by a national committee (North Rhine-Westphalia, Germany).

2.2.2. Apparatus and materials

Pigeons were trained and tested in a touch-screen operant chamber (36 × 33 × 34 cm³), illuminated by a house light and equipped with a feeder. Stimuli with the size of 5 × 5 cm² were presented on the touch-screen fixed to the back of the chamber. Programs for the experimental sessions and the performance of the pigeons were controlled by the MATLAB-Biopsy Toolbox (Rose et al., 2008). For the monocular sessions, rings of Velcro were fixed to the skin around the pigeons' eyes. This way, eye caps made of cardboard could easily be attached to the Velcro rings thereby fully covering the eyes. Pigeons were trained on color patterns, which consisted of a white and a colored (yellow, magenta, cyan or violet) half (Fig. 7). For (conflict) test trials, the colors were combined, so that the stimuli consisted of two colors each filling one half of the image (Fig. 7).

2.2.3. Behavioral task

In an autoshaping procedure naive pigeons learned that pecking on a white stimulus resulted in food delivery. Afterwards, animals were trained on a paradigm similar to the one used in (Ünver and Güntürkün, 2014). In a forced choice task, pigeons had to discriminate the above described stimuli under monocular seeing conditions (Fig. 7). Each eye was trained with a different pair of stimuli whereby positive and negative colors had been randomized between pigeons and eyes. Pecking on the positive stimulus (S+) resulted in a 3 s access to food while pecking on the negative stimulus (S-) resulted in a time out of 2 s with the house light turned off. No peck within 10 s of stimulus presentation also resulted in punishment of a 2 s time out without light. An 8 s inter-trial interval followed each trial. As animals decreased their pecking rate during testing session, for the second run of animals ($n=10$) a variable reward ratio was introduced. Here, animals receive a food reward only in 90% or correct responded trials. Every training session consisted of sixty trials and the animals were trained monocular trained till they reached learning criterion. Thereby the side of the covered eye alternated between days. Criterion was defined as performance above 75% discrimination accuracy within four consecutive sessions, which means that both eyes had to reach 75% correct choices two times in a row. During

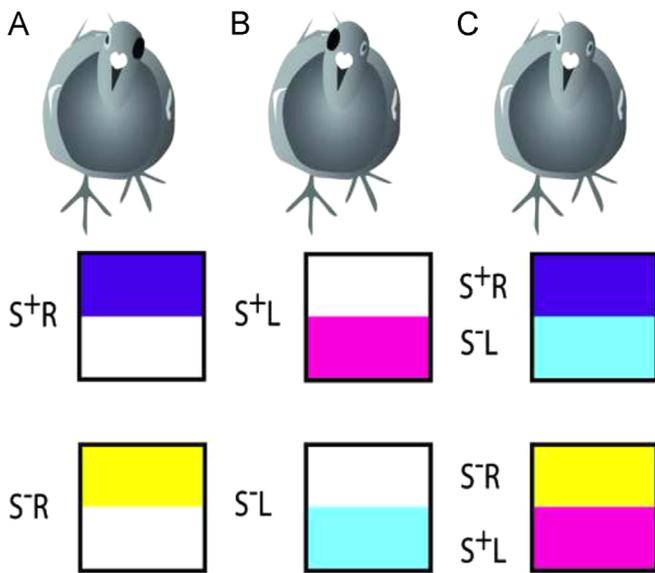


Fig. 7. Metacontrol task. Two stimulus pairs consisting of an S+ and an S− each were learned. One stimulus-pair was trained with the left eye occluded (A), the other pair with the right eye occluded (B). After reaching learning criterion, the animals were tested binocularly with compound stimuli. They had to choose either the S+ of the right eye combined with the S− of the left eye or the S+ of the left eye combined with the S− of the right eye (C). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

the test sessions, no eye was covered, hence the animals performed binocularly. The sessions consisted of fifteen test trials with the above described conflict stimuli interspersed into thirty-five trials with just one white stimulus, a peck to which was rewarded. On test trials, the S+ of one eye was combined with the S− of the other eye and vice versa (Fig. 7). Both configurations were presented simultaneously one on each pecking key and the pigeons had to decide for one of them. These decisions were neither punished nor rewarded. Pecking just stopped the stimulus presentation and started the next trial. If the animal did not peck, the next trial started after 20 s. In between test sessions, the pigeons got six days of training (training stimuli under monocular conditions) and two resting days.

2.2.4. Surgery

After the pigeons had reached more than 50% of correct choices during training sessions, double canulae (Double 9 mm lengths, 2 mm distance, PlasticsOne) were implanted in the HA of both hemispheres. The coordinates (AP 11.0, ML 1.5 and DV 2.0) were taken from the stereotactic atlas of pigeons of (Karten and Hodos, 1967). For surgery animals were anaesthetized with 1 ml per kg of a 7:3 mixture of ketamine (Ketavet, Pharmacia & Upjohn, Erlangen, Germany) and Xylazine (Rompun, Bayer). The skin on the pigeons' head was pulled sideward and the cranial bone cleaned. Two small holes were drilled above the HA and the cannula was placed inside. At last, the cannula was fixed with dental acrylic (Paladur, Nordenta, Hamburg, Germany) and screws were drilled into the skull. If needed the incision was sutured close. After one week of recovery pigeons went back to training.

2.2.5. Pharmacological inhibition

The first test session was conducted without any pharmacological manipulation. Starting with the second test session pigeons received microinjections either of Tetrodotoxin (TTX, 10 ng/ μ l, Tocris) or saline into the left or right HA. The order of injected hemisphere and injected substance was randomized. TTX injections were conducted twice for each hemisphere while saline was

only injected once in each hemisphere.

The Infusion pump (Harvard Apparatus PHD 2000 Syringe) electrically pumped 1 μ l of TTX or saline with an infuse rate of 0.2 μ l/min into the target area. 5 minutes after injection animals were put in the operant chamber to perform the behavioral test.

2.2.6. Histology

After finishing their last test trial, animals were injected with 1 μ l TTX in the HA of both hemispheres and immediately perfused with 4% paraformaldehyde. The brains were postfixed and embedded with gelatin. They were cut in 40 μ m frontal slices and every second slice was stained with an antibody against TTX (Hawaii Biotech Inc.) (Freund et al., 2010). Finally an additional Nissl staining was conducted.

2.2.7. Analysis

Statistical analysis was conducted with Statistica 12.0 (StatSoft). The number of responses on the compound stimuli composed of the S+ of the right eye and the S− of the left eye (S+R) and stimuli consisting of the S+ of the left eye and the S− of the right eye (S+L) (Fig. 7) was compared using two-sided paired *t*-test. In the following sessions with injections the mean of the two injections with TTX in the left and in the right HA as well as the mean of the saline injection in the left and right HA were calculated. For the four injection groups (no injection, TTX left, TTX right, saline) the number of the decisions for the S+L and S+R was compared using ANOVA with repeated measures and two dependent variables: injection group and stimulus (S+L, S+R). Furthermore the asymmetry index for the decisions for the two stimuli was calculated with the following formula: $(\text{number of decisions for S+L} - \text{number of decisions for S+R}) / (\text{number of decisions for S+L} + \text{number of decisions for S+R})$. ANOVA with repeated measures and the factor injection group was conducted. Two sided paired *t*-tests were used as posthoc test for the ANOVAs.

2.3. Results

Discrimination performance during learning was significantly higher with the right eye ($M=69.7\%$, $SD=12.2$) than with the left eye ($M=59.9$, $SD=17.3$) ($t(19)=2.7$; $p=0.013$). Once the learning criterion was reached, however, the discrimination performance did not significantly differ between right ($M=86.9\%$, $SD=5.6$) and left eye ($M=84.4\%$, $SD=7.3$) ($t(19)=1.2$; $p=0.238$).

After training, the pigeons were confronted with the compound stimuli. During the 15 probe trials, animals decided in average 8.4 ± 3.1 times for the S+R and in average 5.5 ± 2.5 times for the S+L (Fig. 8). Thus, they decided significantly more often for the S+R ($t(19)=2.49$; $p=0.022$) (Fig. 8A).

When pigeons' HA was injected with either TTX or saline, the decisions for one stimulus were significantly influenced by the injection condition (no, saline, TTX left, TTX right) ($F(3,57)=3.400$; $p=0.024$) modified by stimulus type (S+R, S+L) (injection \times stimulus interaction: $F(3,57)=2.378$; $p=0.079$). Post-hoc analysis showed that the decisions on the S+L were significantly reduced after TTX injection in the left HA ($M=5.875$; $SD=4.00$) compared to no-injection ($M=8.45$; $SD=5.5$) (t -test: $t(19)=-2.478$, $p=0.023$) and hence, did not differ from decisions on S+R (Fig. 8A).

Comparing asymmetries of left- and right-hemispheric choices demonstrated a significant influence of the injection condition ($F(3,57)=3.15$; $p=0.03$) with the TTX injection in the left HA showing a significantly lower index ($M=-0.08$; $SD=0.58$) compared to no injection ($M=0.19$; $SD=0.38$), saline injection ($M=0.23$; $SD=0.58$) and TTX injection right ($M=0.18$; $SD=0.54$) (posthoc *t*-test $p < 0.05$) (Fig. 8B).

Histological analysis evaluated correct positioning of the

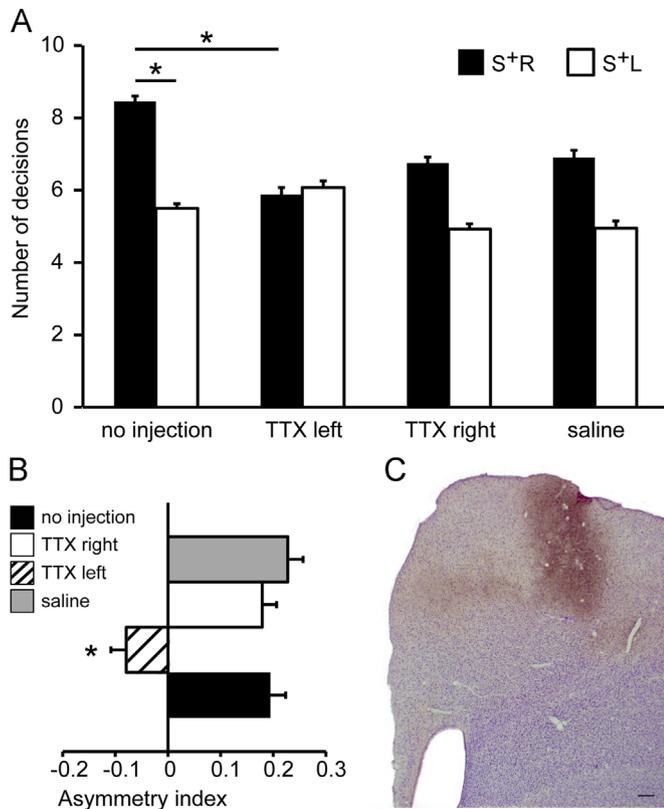


Fig. 8. Metacontrol results. When presented with compound stimuli animals decided more often for the S+ of the right eye (S+R). TTX injected into the left HA reduced decisions for the S+R (A). Thus the asymmetry index for the decisions significantly differed after TTX injections in the left HA compared to no injection, saline injection and TTX injected into the left HA (B). Immunostaining against TTX showed that the HA was affected (C). Mean and SE are presented in A+B; * $p < 0.05$; bar in C represents 200 μm.

cannulae and the extent of TTX diffusion. Immunostaining demonstrated that the cannulae were not plugged at the end of the experiments and that TTX had diffused in the lateral part of HA and in the medial parts of the HI and HD (Fig. 8C).

2.4. Discussion

The study revealed that the left hemisphere of pigeons is able to dominate the right hemisphere in conflict situations that induce converse response tendencies of the hemispheres. Thus, when confronted with conflicting stimuli animals decided more often for the stimulus that was learnt with the right eye. This response pattern suggests that conflict choices were dominated by the left hemisphere and are in line with several findings of a dominance of the left hemisphere. The left hemisphere performs better in complex discrimination tasks (Güntürkün and Kesch, 1987; Letzner et al., 2014), is dominant in visuomotor control (Güntürkün and Hoferichter, 1985) and has better access to information from both eyes (Letzner et al., 2014; Nottelmann et al., 2002; Valencia-Alfonso et al., 2009). Moreover, associative learning increases discriminatory neuronal activity between a rewarded and unrewarded stimulus within the left visual forebrain (Verhaal et al., 2012). Thus, when processing the conflict stimuli that are composed of the S+ for one and the S− of the other eye, association strength for the S+ as well as S− should be superior in the left compared to the right hemisphere. As a consequence, the left hemisphere might be able to dominate choice behavior. The influence of past experience onto conflict decisions is (likely) mediated by top-down mechanisms arising from the left wulst as

indicated by our experiments.

When left-wulst activity is silenced, dominance in decisions for the left hemisphere stimulus is lost. This is not caused by a decrease in general responses of the pigeons. Pigeons are able to solve simple discrimination tasks even if their wulst is lesioned (Parker and Delius, 1980). The only advantage they have from an intact wulst is that they are faster in decision making (Parker and Delius, 1980). But as soon as the task becomes more complex and changes in value of the stimuli have to be considered, pecking responses depend on an intact wulst (Pasternak, 1977; Shimizu and Hodos, 1989). Accordingly, enhanced knowledge about stimulus values in the left hemisphere is mediated by the left wulst that in turn controls balance of left- and right hemispheric decisions in our metacontrol experiment. While blocking the neuronal activity of the right wulst had no effect, blocking of the left wulst decreased decisions for the left hemisphere stimulus. This result pattern is well in line with our electrophysiological findings showing that top-down modulation from the left wulst on visual information processing in the left Rt is stronger than in the right hemisphere.

3. General discussion

We departed from the observation that in a large number of animals that reach from chicken to humans, a left hemispheric superiority in the categorization of some stimulus classes are observed. Given our knowledge on several neurobiological aspects of left hemispheric categorization in pigeons, we aimed to test the possibility that left–right differences of top-down control could constitute the critical neural entity for the left hemispheric categorization superiority in this species. Indeed, we discovered that the visual wulst of the left telencephalon exerts a strong modulatory influence on single cells of the left thalamic Rt. By this top-down projection, ascending visual pathways can possibly be modified according to past experience or attentional needs. Consequently, we could show in a second study that pigeons primarily select the stimulus that had been learned by the left hemisphere. Transient inactivation of the left wulst abolished this asymmetry of choice. Thus, our results make it likely that the superiority in visual discrimination and categorization in pigeons could be related at least in part to asymmetries of top-down modulation.

Several recent studies could indeed reveal that asymmetries of cortical top-down signals are related to the categorization of various stimulus types in the visual or in the auditory domain (Angenstein and Brechmann, 2013; Coutanche and Thompson-Schill, 2014). These studies suggest that lateralized top-down architecture can determine both the engagement and disengagement of downstream structures and thereby plays an important role for setting the state of sensory regions to optimize processing (Haegens et al., 2011). This possibly happens by learning of category specific features that are then pre-activated in downstream visual structures that process early vision (Ullman, 2007). Indeed, psychophysical studies in humans and monkeys have shown that category-specific features are acquired during learning in the visual system in the course of training (Schyns and Rodet, 1997; Sigala et al., 2002). As a result, an increased selectivity to features that support categorization tasks can modulate vision in a top-down manner (Sigala and Logothetis, 2002).

The wulst is the primary visual projection area of the ascending thalamofugal pathway. The wulst is also the source of the largest pallial descending fiber system, the TSM. The TSM does not directly reach the Rt, but modulates tectal systems, which then project onto the Rt. TSM-terminals are primarily found in tectal lamina 13 where they contact tectorotundal neurons (Miceli and Repérant, 1985). Thus, the impact of wulst anesthesia on Rt-

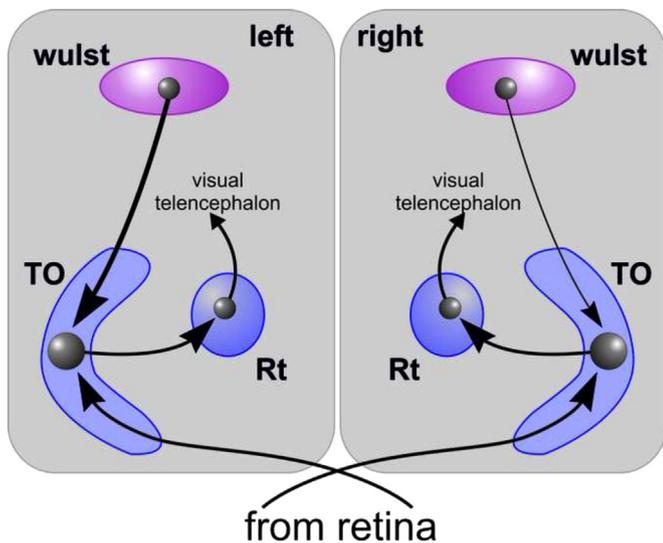


Fig. 9. Hypothetical functional diagram of the present result pattern. It is assumed that the asymmetry discovered in experiment 1 is not primarily due to left right differences of bottom-up pathways. It is instead possible that the top-down synaptic transmission between the wulst and the tectum is more effective on the left side and thus modulates the ascending visual pathways in lateralized manner. Abbreviations: n. rotundus (Rt), tectum opticum (TO).

neurons is probably relayed via tectorotundal neurons of lamina 13. Since this tectorotundal system is also monosynaptically activated by the contralateral retina (Hardy et al., 1984), tectorotundal cells of lamina 13 constitute a nodal point of integration of ascending and descending pathways (see Fig. 1).

Since the number of telencephalotectal neurons within TSM is about equal between left and right (Manns et al., 2007), the differences observed in the present study do not derive from quantitative differences in the number of descending axons but from differences in synaptic weights along this pathway. This is in accordance with the observation of the present study that the number of WMRs does not differ between left and right, although the left wulst has a significantly higher impact on rotundal processing (Fig. 9). Thus, asymmetries of top-down processing may not necessarily be prewired but emerge during learning or due to ontogenetic experiences (Manns and Ströckens, 2014) and are coded in terms of synaptic strengths. As outlined above, this could be the reason why newly hatched chicks develop a left hemispheric superiority in categorization during a period of learning (Howard et al., 1980; Rogers and Anson, 1979; Rogers et al., 2007). At the same time, such a wiring pattern can explain why under conditions of metacontrol, the left hemisphere has a higher probability to dominate the response, although both hemispheres have in principle a similar learning history.

Our findings have potentially also an interesting implication for the right hemisphere in birds. If the right tectofugal system is less modified by top-down systems, it could transmit visual information that is less modified by past experience. This could be the reason why it is the right hemispheric visual system that directly after hatch dominates inborn behavioral response patterns towards sexual or agonistic cues (Bullock and Rogers, 1992; Dharmaretnam and Rogers, 2005). These right hemispheric response biases towards possibly inborn stimulus patterns are also visible in amphibians (Lippolis et al., 2002), reptiles (Deckel, 1995), and mammals (Casperd and Dunbar, 1996). It is yet an open question if these asymmetries in other species result from a wiring pattern as discovered in birds. However, we are inclined to believe that left-differences of top-down signaling not only modify the circuits in one hemisphere, but always create complementary modes of processing in the other.

Acknowledgements

OG: supported by the DFG through SFB874 and Gu 227/16-1. We thank Jessica Kocon and Miriam Schlott for their help with data collection.

References

- Adam, R., Güntürkün, O., 2009. When one hemisphere takes control: metacontrol in pigeons (*Columba livia*). *PLoS ONE* 4, e5307. <http://dx.doi.org/10.1371/journal.pone.0005307>.
- Alonso, Y., 1998. Lateralization of visual guided behaviour during feeding in zebra finches (*Taeniopygia guttata*). *Behav. Process.* 43, 257–263.
- Andresen, D.R., Marsolek, C.J., 2005. Does a causal relation exist between the functional hemispheric asymmetries of visual processing subsystems? *Brain Cogn.* 59, 135–144.
- Angenstein, N., Brechmann, A., 2013. Division of labor between left and right human auditory cortices during the processing of intensity and duration. *Neuroimage* 83, 1–11.
- Bullock, S.P., Rogers, L.J., 1992. Hemispheric specialization for the control of copulation in the young chick and effects of 5 alpha-dihydrotestosterone and 17 beta-oestradiol. *Behav. Brain Res.* 48, 9–14.
- Casperd, J.M., Dunbar, R.I.M., 1996. Asymmetries in the visual processing of emotional cues during agonistic interactions by gelada baboons. *Behav. Process.* 37, 57–65.
- Catania, A.C., 1965. Interocular transfer of discriminations in the pigeon. *J. Exp. Anal. Behav.* 8, 147–155.
- Coutanche, M.N., Thompson-Schill, S.L., 2014. Creating concepts from converging features in human cortex. *Cereb. Cortex* (N.Y. N 1991). <http://dx.doi.org/10.1093/cercor/bhu057>.
- Dépy, D., Fagot, J., Vauclair, J., 1998. Comparative assessment of distance processing and hemispheric specialization in humans and baboons (*Papio papio*). *Brain Cogn.* 38, 165–182. <http://dx.doi.org/10.1006/brcg.1998.1027>.
- Deckel, A.W., 1995. Laterality of aggressive responses in anolis. *J. Exp. Zool.* 272, 194–200.
- Dharmaretnam, M., Rogers, L.J., 2005. Hemispheric specialization and dual processing in strongly versus weakly lateralized chicks. *Behav. Brain Res.* 162, 62–70. <http://dx.doi.org/10.1016/j.bbr.2005.03.012>.
- Folta, K., Diekamp, B., Güntürkün, O., 2004. Asymmetrical modes of visual bottom-up and top-down integration in the thalamic nucleus rotundus of pigeons. *J. Neurosci. Off. J. Soc. Neurosci.* 24, 9475–9485. <http://dx.doi.org/10.1523/JNEUROSCI.3289-04.2004>.
- Freund, N., Manns, M., Rose, J., 2010. A method for the evaluation of intracranial tetrodotoxin injections. *J. Neurosci. Methods* 186, 25–28.
- Güntürkün, O., 1985. Lateralization of visually controlled behavior in pigeons. *Physiol. Behav.* 34, 575–577.
- Güntürkün, O., 1997. Avian visual lateralization – a review. *NeuroReport* 8 (6), iii–xi.
- Güntürkün, O., 2000. Sensory physiology: vision. *Sturkie's Avian Physiology*, pp. 1–19.
- Güntürkün, O., Hoferichter, H.H., 1985. Neglect after section of a left telencephalotectal tract in pigeons. *Behav. Brain Res.* 18, 1–9.
- Güntürkün, O., Kesch, S., 1987. Visual lateralization during feeding in pigeons. *Behav. Neurosci.* 101, 433–435.
- Güntürkün, O., Hahmann, U., 1999. Functional subdivisions of the ascending visual pathways in the pigeon. *Behav. Brain Res.* 98, 193–201.
- Güntürkün, O., Hellmann, B., Melsbach, G., Prior, H., 1998. Asymmetries of representation in the visual system of pigeons. *NeuroReport* 9, 4127–4130.
- Güntürkün, O., Diekamp, B., Manns, M., Nottelmann, F., Prior, H., Schwarz, A., Skiba, M., 2000. Asymmetry pays: visual lateralization improves discrimination success in pigeons. *Curr. Biol. CB* 10, 1079–1081.
- Haegens, S., Händel, B.F., Jensen, O., 2011. Top-down controlled alpha band activity in somatosensory areas determines behavioral performance in a discrimination task. *J. Neurosci* 31, 5197–5204.
- Hardy, O., Leresche, N., Jassik-Gerschenfeld, D., 1984. Postsynaptic potentials in neurons of the pigeon's optic tectum in response to afferent stimulation from the retina and other visual structures: an intracellular study. *Brain Res.* 311, 65–74.
- Howard, K.J., Rogers, L.J., Boura, A.L., 1980. Functional lateralization of the chicken forebrain revealed by use of intracranial glutamate. *Brain Res.* 188, 369–382.
- Jason, G.W., Cowey, A., Weiskrantz, L., 1984. Hemispheric asymmetry for a visuo-spatial task in monkeys. *Neuropsychologia* 22, 777–784.
- Karten, H.J., Hodos, W., 1967. *A Stereotaxic Atlas of the Brain of the Pigeon (Columba Livia)*. John Hopkins Press, Baltimore, Maryland.
- Kavcic, V., Fei, R., Hu, S., Doty, R.W., 2000. Hemispheric interaction, metacontrol, and mnemonic processing in split-brain macaques. *Behav. Brain Res.* 111, 71–82.
- Koivisto, M., Revonsuo, A., 2003. Object recognition in the cerebral hemispheres as revealed by visual field experiments. *Later. Asymmetries Body Brain Cogn.* 8, 135–153. <http://dx.doi.org/10.1080/713754482>.
- Laeng, B., Zarrinpar, A., Kosslyn, S.M., 2003. Do separate processes identify objects as exemplars versus members of basic-level categories? Evidence from hemispheric specialization. *Brain Cogn.* 53, 15–27.

- Larkum, M.E., Senn, W., Lüscher, H.-R., 2004. Top-down dendritic input increases the gain of layer 5 pyramidal neurons. *Cereb. Cortex* (N.Y. N 1991) 14, 1059–1070. <http://dx.doi.org/10.1093/cercor/bhh065>.
- Lazarus-Mainka, G., Hörmann, H., 1978. Strategic selection (metacognition) of hemisphere dominance in normal human subjects, or: some neglected factors in laterality research. *Psychol. Res.* 40, 15–25.
- Letzner, S., Patzke, N., Verhaal, J., Manns, M., 2014. Shaping a lateralized brain: asymmetrical light experience modulates access to visual interhemispheric information in pigeons. *Sci. Rep.* 4, 4253. <http://dx.doi.org/10.1038/srep04253>.
- Levy, J., Trevarthen, C., 1976. Metacognition of hemispheric function in human split-brain patients. *J. Exp. Psychol. Hum. Percept. Perform.* 2, 299–312.
- Lippolis, G., Bisazza, A., Rogers, L.J., Vallortigara, G., 2002. Lateralisation of predator avoidance responses in three species of toads. *Laterality* 7, 163–183.
- Manns, M., Güntürkün, O., 1999. Monocular deprivation alters the direction of functional and morphological asymmetries in the pigeon's (*Columba livia*) visual system. *Behav. Neurosci.* 113, 1257–1266.
- Manns, M., Römling, J., 2012. The impact of asymmetrical light input on cerebral hemispheric specialization and interhemispheric cooperation. *Nat. Commun.* 3, 696. <http://dx.doi.org/10.1038/ncomms1699>.
- Manns, M., Ströckens, F., 2014. Functional and structural comparison of visual lateralization in birds—similar but still different. *Front. Psychol.* 5, 206. <http://dx.doi.org/10.3389/fpsyg.2014.00206>.
- Manns, M., Freund, N., Güntürkün, O., 2008. Development of the diencephalic relay structures of the visual thalamofugal system in pigeons. *Brain Res. Bull.* 75, 424–427. <http://dx.doi.org/10.1016/j.brainresbull.2007.10.036>.
- Manns, M., Freund, N., Patzke, N., Güntürkün, O., 2007. Organization of telencephalotectal projections in pigeons: impact for lateralized top-down control. *Neuroscience* 144, 645–653. <http://dx.doi.org/10.1016/j.neuroscience.2006.09.043>.
- Marsolek, C.J., 1999. Dissociable neural subsystems underlie abstract and specific object recognition. *Psychol. Sci.* 10, 111–118. <http://dx.doi.org/10.1111/1467-9280.00117>.
- Martin, R., Houssemand, C., Schiltz, C., Burnod, Y., Alexandre, F., 2008. Is there continuity between categorical and coordinate spatial relations coding? Evidence from a grid/no-grid working memory paradigm. *Neuropsychologia* 46, 576–594. <http://dx.doi.org/10.1016/j.neuropsychologia.2007.10.010>.
- McMenamin, B.W., Deason, R.G., Steele, V.R., Koutstaal, W., Marsolek, C.J., 2015. Separability of abstract-category and specific-exemplar visual object subsystems: evidence from fMRI pattern analysis. *Brain Cogn.* 93, 54–63. <http://dx.doi.org/10.1016/j.bandc.2014.11.007>.
- Miceli, D., Repérant, J., 1985. Telencephalic afferent projections from the diencephalon and brainstem in the pigeon. A retrograde multiple-label fluorescent study. *Exp. Biol.* 44, 71–99.
- Miceli, D., Repérant, J., Villalobos, J., Dionne, L., 1987. Extratelencephalic projections of the avian visual Wulst. A quantitative autoradiographic study in the pigeon *Columbia livia*. *J. Hirnforsch.* 28, 45–57.
- Nottelmann, F., Wohlschläger, A., Güntürkün, O., 2002. Unihemispheric memory in pigeons—knowledge, the left hemisphere is reluctant to share. *Behav. Brain Res.* 133, 309–315.
- Ocklenburg, S., Güntürkün, O., 2012. Hemispheric asymmetries: the comparative view. *Front. Psychol.* 3, 5. <http://dx.doi.org/10.3389/fpsyg.2012.00005>.
- Ocklenburg, S., Ströckens, F., Güntürkün, O., 2013. Lateralisation of conspecific vocalisation in non-human vertebrates. *Laterality* 18, 1–31. <http://dx.doi.org/10.1080/1357650X.2011.626561>.
- Palermo, L., Bureca, I., Matano, A., Guariglia, C., 2008. Hemispheric contribution to categorical and coordinate representational processes: a study on brain-damaged patients. *Neuropsychologia* 46, 2802–2807. <http://dx.doi.org/10.1016/j.neuropsychologia.2008.05.020>.
- Palmers, C., Zeier, H., 1974. Hemispheric dominance and transfer in the pigeon. *Brain Res.* 76, 537–541.
- Parker, D.M., Delius, J.D., 1980. The effects of wulst lesions on simple visual discrimination performance in the pigeon. *Behav. Process.* 5, 151–159.
- Pasternak, T., 1977. Delayed matching performance after visual Wulst lesions in pigeons. *J. Comp. Physiol. Psychol.* 91, 472–484.
- Prior, H., Wiltshko, R., Stapput, K., Güntürkün, O., Wiltshko, W., 2004. Visual lateralization and homing in pigeons. *Behav. Brain Res.* 154, 301–310.
- Reiner, A., Karten, H.J., 1983. The laminar source of efferent projections from the avian Wulst. *Brain Res.* 275, 349–354.
- Roelfsema, P.R., Tolboom, M., Khayat, P.S., 2007. Different processing phases for features, figures, and selective attention in the primary visual cortex. *Neuron* 56, 785–792. <http://dx.doi.org/10.1016/j.neuron.2007.10.006>.
- Roelfsema, P.R., Lamme, V.A.F., Spekreijse, H., Bosch, H., 2002. Figure-ground segregation in a recurrent network architecture. *J. Cogn. Neurosci.* 14, 525–537. <http://dx.doi.org/10.1162/089989290260045756>.
- Rogers, L.J., Anson, J.M., 1979. Lateralisation of function in the chicken fore-brain. *Pharmacol. Biochem. Behav.* 10, 679–686.
- Rogers, L.J., Andrew, R.J., Johnston, A.N.B., 2007. Light experience and the development of behavioural lateralization in chicks III. Learning to distinguish pebbles from grains. *Behav. Brain Res.* 177, 61–69. <http://dx.doi.org/10.1016/j.bbr.2006.11.002>.
- Rose, J., Otto, T., Dittrich, L., 2008. The Biopsychology-Toolbox: a free, open-source Matlab-toolbox for the control of behavioral experiments. *J. Neurosci. Methods* 175, 104–107. <http://dx.doi.org/10.1016/j.jneumeth.2008.08.006>.
- Saleh, C.N., Ehrlich, D., 1984. Composition of the supraoptic decussation of the chick (*Gallus gallus*). A possible factor limiting interhemispheric transfer of visual information. *Cell Tissue Res.* 236, 601–609.
- Schyns, P.G., Rodet, L., 1997. Categorization creates functional features. *J. Exp. Psychol. Learn. Mem. Cogn.* 23, 681–696.
- Shimizu, T., Hodos, W., 1989. Reversal learning in pigeons: effects of selective lesions of the Wulst. *Behav. Neurosci.* 103, 262–272.
- Sigala, N., Logothetis, N.K., 2002. Visual categorization shapes feature selectivity in the primate temporal cortex. *Nature* 415, 318–320.
- Sigala, N., Gabbiani, F., Logothetis, N.K., 2002. Visual categorization and object representation in monkeys and humans. *J. Cogn. Neurosci.* 14, 187–198.
- Ströckens, F., Güntürkün, O., Ocklenburg, S., 2013. Limb preferences in non-human vertebrates. *Laterality* 18, 536–575. <http://dx.doi.org/10.1080/1357650X.2012.723008>.
- Ullman, S., 2007. Object recognition and segmentation by a fragment-based hierarchy. *Trends Cogn. Sci.* 11, 58–64. <http://dx.doi.org/10.1016/j.tics.2006.11.009>.
- Ünver, E., Güntürkün, O., 2014. Evidence for interhemispheric conflict during metacognition in pigeons. *Behav. Brain Res.* 270, 146–150. <http://dx.doi.org/10.1016/j.bbr.2014.05.016>.
- Urgesi, C., Bricolo, E., Aglioti, S.M., 2005. Hemispheric metacognition and cerebral dominance in healthy individuals investigated by means of chimeric faces. *Brain Res. Cogn. Brain Res.* 24, 513–525. <http://dx.doi.org/10.1016/j.cogbrainres.2005.03.005>.
- Valencia-Alfonso, C.E., Verhaal, J., Güntürkün, O., 2009. Ascending and descending mechanisms of visual lateralization in pigeons. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 364, 955–963.
- Valenti, A., Sovrano, V.A., Zucca, P., Vallortigara, G., 2003. Visual lateralisation in quails (*Coturnix coturnix*). *Laterality* 8, 67–78.
- Vallortigara, G., 2000. Comparative neuropsychology of the dual brain: a stroll through animals' left and right perceptual worlds. *Brain Lang.* 73, 189–219. <http://dx.doi.org/10.1006/brln.2000.2303>.
- Vallortigara, G., Rogers, L.J., 2005. Survival with an asymmetrical brain: advantages and disadvantages of cerebral lateralization. *Behav. Brain Sci.* 28, 575–589. <http://dx.doi.org/10.1017/S0140525X05000105>, discussion 589–633.
- Vallortigara, G., Cozzutti, C., Tommasi, L., Rogers, L.J., 2001. How birds use their eyes: Opposite left-right specialization for the lateral and frontal visual hemifield in the domestic chick. *Curr. Biol.* 11, 29–33.
- Van der Ham, I.J.M., Raemaekers, M., van Wezel, R.J.A., Oleksiak, A., Postma, A., 2009. Categorical and coordinate spatial relations in working memory: an fMRI study. *Brain Res.* 1297, 70–79. <http://dx.doi.org/10.1016/j.brainres.2009.07.088>.
- Van der Ham, I.J.M., van Wezel, R.J.A., Oleksiak, A., van Zandvoort, M.J.E., Frijns, C.J.M., Kappelle, L.J., Postma, A., 2012. The effect of stimulus features on working memory of categorical and coordinate spatial relations in patients with unilateral brain damage. *Cortex J. Devoted Study Nerv. Syst. Behav.* 48, 737–745. <http://dx.doi.org/10.1016/j.cortex.2011.03.002>.
- Verhaal, J., Kirsch, J.A., Vlachos, I., Manns, M., Güntürkün, O., 2012. Lateralized reward-related visual discrimination in the avian entopallium. *Eur. J. Neurosci.* 35, 1337–1343. <http://dx.doi.org/10.1111/j.1460-9568.2012.08049.x>.
- Vogels, R., Saunders, R.C., Orban, G.A., 1994. Hemispheric lateralization in rhesus monkeys can be task-dependent. *Neuropsychologia* 32, 425–438.
- Von Fersen, L., Güntürkün, O., 1990. Visual memory lateralization in pigeons. *Neuropsychologia* 28, 1–7.
- Yamazaki, Y., Aust, U., Huber, L., Hausmann, M., Güntürkün, O., 2007. Lateralized cognition: asymmetrical and complementary strategies of pigeons during discrimination of the “human concept”. *Cognition* 104, 315–344.