Modulation of alpha oscillations by attention is predicted by hemispheric asymmetry of subcortical regions.

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Abstract

Evidence suggests that subcortical structures play a role in high-level cognitive functions such as the allocation of spatial attention. While there is abundant evidence in humans for posterior alpha band oscillations being modulated by spatial attention, little is known about how subcortical regions contribute to these oscillatory modulations, particularly under varying conditions of cognitive challenge. In this study, we combined MEG and structural MRI data to investigate the role of subcortical structures in controlling the allocation of attentional resources by employing a cued spatial attention paradigm with varying levels of perceptual load. We asked whether hemispheric lateralization of volumetric measures of the thalamus and basal ganglia predicted the hemispheric modulation of alpha-band power. Lateral asymmetry of the globus pallidus, caudate nucleus, and thalamus predicted attention-related modulations of posterior alpha oscillations. When the perceptual load was applied to the target and the distractor was salient caudate nucleus asymmetry predicted alpha-band modulations. Globus Pallidus was predictive of alpha-band modulations when either the target had a high load, or the distractor was salient, but not both. Finally, the asymmetry of the thalamus predicted alpha band modulation when neither component of the task was perceptually demanding. In addition to delivering new insight into the subcortical circuity controlling alpha oscillations with spatial attention, our finding might also have clinical applications. We provide a framework that could

be followed for detecting how structural changes in subcortical regions that are associated with neurological disorders can be reflected in the modulation of oscillatory brain activity.

Introduction

The visual world provides more sensory information than we can be aware of at any given moment. Thus, our brains must prioritise goal-relevant over distracting information. A rich body of research shows that the brain amplifies goal-relevant inputs, and suppresses non-relevant inputs by a process referred to as selective attention (1–3). There is ample evidence for top-down control of neocortical regions associated with sensory processing when information is prioritized (1,4,5). The dorsal attention network, which consists of the intraparietal sulcus/superior parietal lobule, and the frontal eye fields, is the most predominant network associated with the allocation of attention (6–8). However, although the role of neocortex for spatial attention and cognitive control has been extensively studied, the contributions of subcortical regions are less well understood. One reason, amongst many others, is that MEG and EEG are not well suited for detecting subcortical activity. Therefore, the present study aims to provide insights into the contribution of the thalamus and basal ganglia in driving top-down spatial attention.

There has been intense focus on the cortical contributions to the top-down control processes, yet there are multiple sources of evidence to suggest that subcortical structures also play an important role in cognitive control. For instance, it has been shown that the pulvinar plays an important role in the modulation of neocortical alpha oscillations associated with the allocation of attention (9). The basal ganglia have been demonstrated to be involved in various types of cognitive control, including attention (10,11), behavioral output (12), and conscious perception (13). Studies in rats and non-human primates have shown that both the thalamus and superior colliculus, are involved in the control of spatial attention by contributing to the regulation of neocortical activity (Fiebelkorn & Kastner, 2020; Krauzlis et al., 2013, 2018). Notably, when the largest nucleus of the thalamus, the pulvinar, was inactivated after muscimol infusion, the monkey's ability to detect colour changes in attended stimuli was lowered. This behavioral

deficit occurred when the target was in the receptive field of V4 neurons that were connected to lesioned pulvinar (19). The basal ganglia are also involved in visuospatial attention through their connections to cortical areas such as the prefrontal cortex via thalamus. Anatomical tracing studies on selective attention and distractor suppression point to a key role of prefrontal-basal ganglia-thalamus pathway whereby sensory thalamic activity is regulated by prefrontal cortex via basal ganglia (11). Furthermore, fMRI studies in humans demonstrated increased activation in basal ganglia when covert attention was reallocated. Additionally, dynamic causal modelling has shown that the basal ganglia can modulate the top-down influence of the prefrontal cortex on the visual cortex in a task-dependent manner (20).

In terms of neuronal dynamics, power modulation of oscillatory activity in the alpha band (8-13Hz) has been proposed to reflect resource allocation between goal-relevant and irrelevant stimuli. This has consistently been shown between studies in EEG and MEG in which attention is allocated to the left or right hemifield. Such studies typically find an alpha power decrease in the hemisphere contralateral to the attended stimuli complemented by a relative increase in alpha power in the other hemisphere associated with unattended stimuli (Okazaki et al., 2014; Thut et al., 2006; Worden et al., 2000). It is debated whether the alpha power associated with the unattended stimuli is under task-driven top-down control or rather explained by an indirect control mechanism driven by the engagement of the target (25). The latter notion is aligned with perception load theory that is defined as the perceptual demand of the task or relevant stimulus, according to which the (finite) resources are allocated (26). Indeed, a recent study demonstrated when the target stimulus has a higher perceptual load (e.g., more difficult to perceive), alpha band power increases in ipsilateral regions thus indirectly reflecting distractor suppression (27).

Based on these findings, both oscillatory activity in the alpha band and the activity of subcortical structures are involved in the allocation of attentional resources. The direct relationship between activity in subcortical regions and neocortical oscillations is poorly understood in humans, in part owing to the difficulty in detecting the activity of deep structures using MEG/EEG. One way around this is to instead investigate, the relationship between the

volumetric measures of subcortical structures and oscillatory brain activity by combining MRI and electrophysiological measures such as MEG. Using this approach, it was shown that the hemispheric lateralized modulation of alpha oscillations is correlated with the volumetric hemispheric asymmetry of both the globus pallidus and the thalamus (28). The relationship between the globus pallidus and the modulation of alpha oscillations was demonstrated in the trials where the visual stimuli were associated with high-value (positive or negative) reward valence.

In this study, we aimed to identify a link between the volumetric asymmetries of subcortical structures and the modulation of alpha oscillations in the context of spatial attention without explicit reward-associations. Given the assumed contribution of the basal ganglia to reward-based learning (29–32), it is perhaps unsurprising to find contributions of the globus pallidus in the paradigms targeting reward valence. What remains to be determined is whether these structures play a more general role in the formation of spatial attention biases. We analysed MEG and structural data from a previous study (27), in which spatial cues guided participants to covertly attend to one stimulus (target) and ignore the other (distractor). Importantly, the target load and the visual saliency of the distractor were manipulated using a noise mask. This load/salience manipulation resulted in four conditions that affect the attentional demands of target and distractor This approach allowed us to relate the hemispheric volumetric asymmetries in thalamus, caudate nucleus, and globus pallidus to the modulation of alpha oscillations when spatial attention is allocated under varying conditions of cognitive challenge.

Results

We investigated the relationship between the volumetric lateralization of subcortical structures estimated from structural MRIs and the hemispheric modulation of alpha oscillations measured by MEG in a spatially cued change detection task. We asked the participants to covertly attend to face-stimuli in the left or right visual field and indicate the direction of a subtle gaze-shift of the attended face (Figure 1A). The influences of perceptual load and distractor salience were

examined by combining noisy and clear target and distractor stimuli in a 2 x 2 design (Figure 1B).

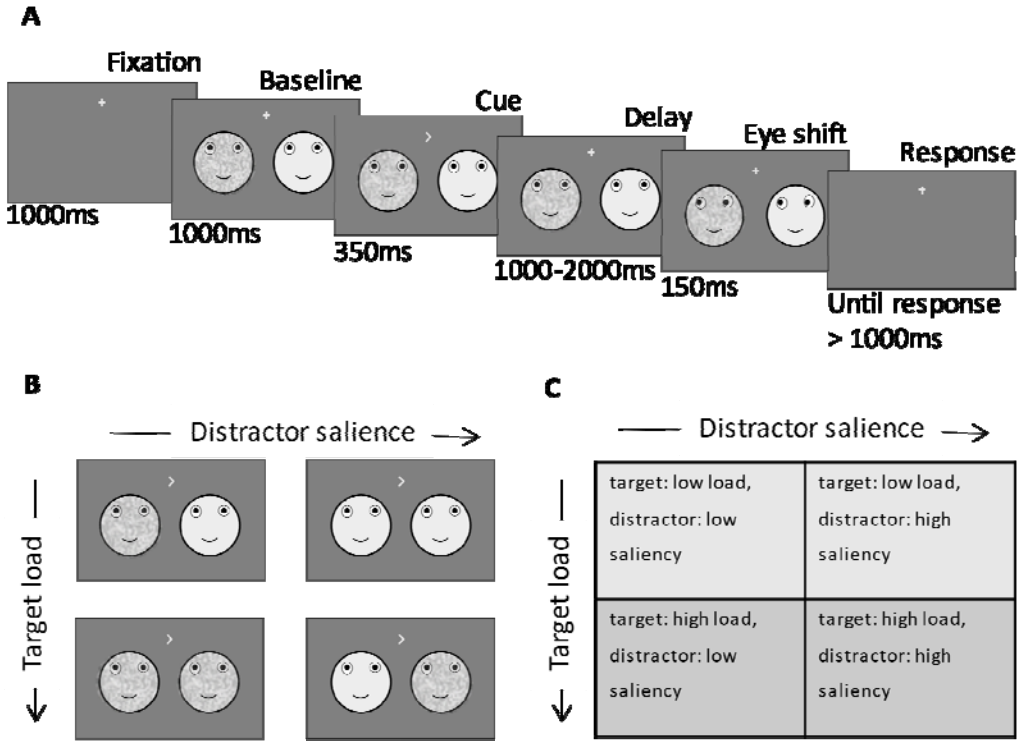

Figure 1. Schematic of experimental design. A. Two face stimuli were presented simultaneously in the left and right hemifield. After baseline, a directional cue indicated the location of the target. After a variable delay interval (1000-2000ms) the eye-gaze of each stimulus (independent of the other) shifted randomly to the right or left. Subjects had to indicate the direction of the target eye movement after the delay interval (the face images have been replaced by emojis for copy right purposes). B. Examples of visual stimuli for each of the four conditions C. Table with the labels of the four load/salience conditions.

Modulation of alpha power with respect to left and right cues

To quantify the anticipatory change in alpha power, we analysed the modulation of power in the -850 – 0 ms interval prior to the target. As expected from a previous report (27), we

observed a power decrease contralateral to the cued hemifield and a relative increase ipsilaterally (i.e. an increase contralateral to the distractor, Figure 2A) As expected, the magnitude of the modulation index (MI(α)) reflecting the relative difference in alpha power when attending left versus right, gradually decreased and increased over respectively the left and right hemisphere until target onset (Figure 2B). We then identified symmetric clusters of sensors (5 over each hemisphere) that showed the highest modulation of alpha power (Figure 2C) and focused the subsequent analyses on these sensors of interest.

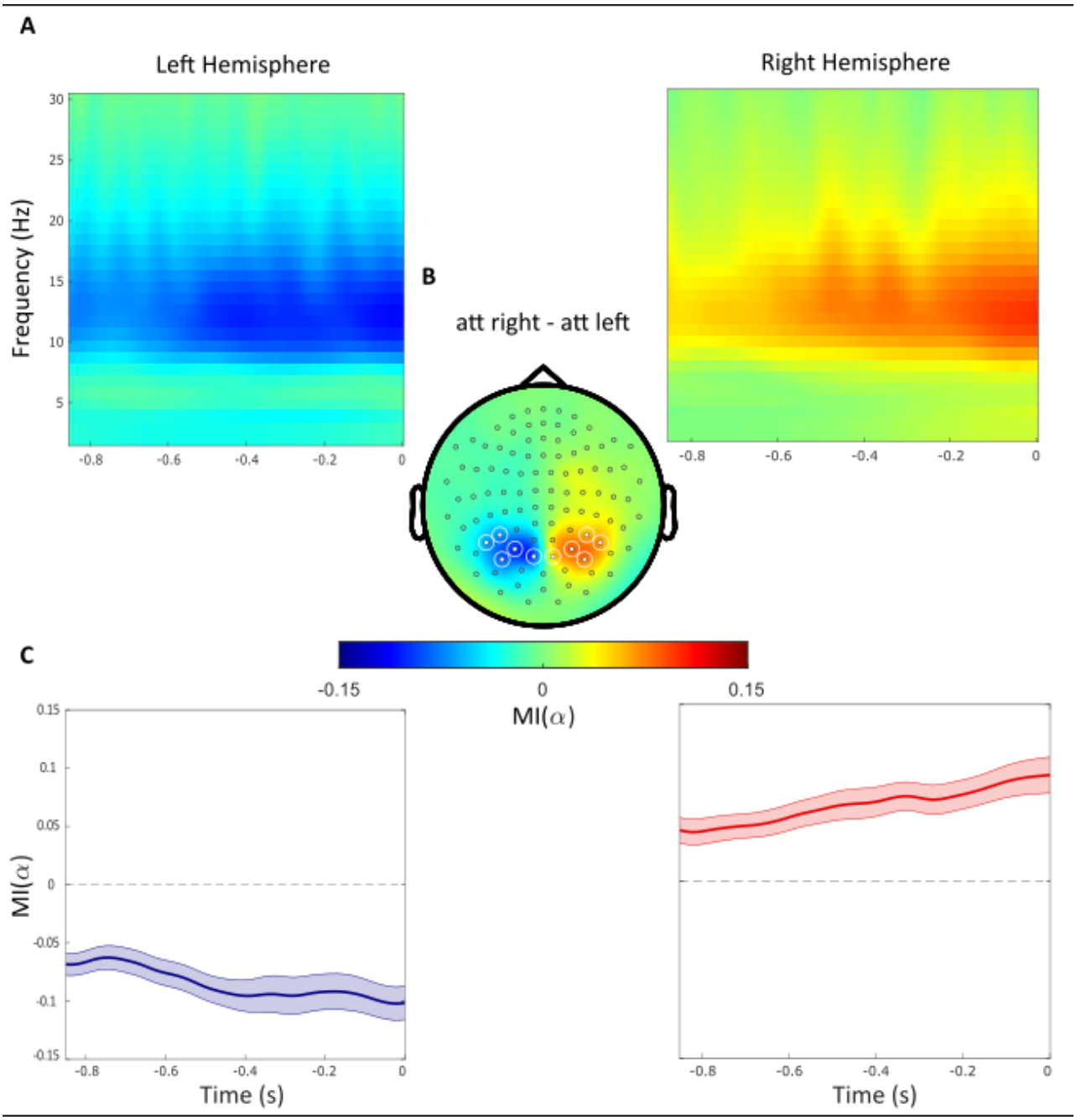

Figure 2. Alpha power decreases contralaterally and increases ipsilaterally with respect to the cued hemifield. A. Time-frequency representations of power demonstrate the difference between attended right versus left trials (t = 0 indicate the target onset). B. Topographical plot of the relative difference between attend right versus left trials. Regions of Interest sensors

(ROIs) are marked with white circles. C. The alpha band modulation (MI(α)) averaged over ROI sensors within the left and right hemispheres, respectively. The absolute MI(α) increased gradually during the delay interval until the onset of the target stimuli.

Hemispheric asymmetry of subcortical regions

Next, we computed the hemispheric lateralization of alpha power modulation in each individual. We did so using the HLM(α) index which quantifies how strongly the alpha power in the left hemisphere is modulated by attention with respect to alpha power modulations in the right hemisphere.

The histogram in figure 3A illustrates the distribution of HLM(α) in all participants. HLM(α) indices range from ~-0.15 to 0.15 and are normally distributed around zero before target onset (Shapiro-Wilk, W = 0.966, p-value = 0.3895).

We then calculated the hemispheric lateralized volumes of the seven subcortical structures, as illustrated in Figure 3B (thalamus, caudate nucleus, putamen, globus pallidus, hippocampus, amygdala, and nucleus accumbens) using the FIRST algorithm on the MRI data. Thalamus (mean ± std = -0.0123 ± 0.0121, p-value < 0.000), putamen (mean ± std = -0.0149 ± 0.0285, p-value = 0.004) and nucleus accumbens (mean ± std = -0.1141 ± 0.0746, p-value < 0.000) have significantly negative LV values (i.e., left lateralization) whereas the caudate nucleus is right lateralized (mean ± std = 0.0115 ± 0.0285, p-value = 0.021) (Figure 3B). Globus pallidus, hippocampus, and amygdala did not show any robust volume lateralization.

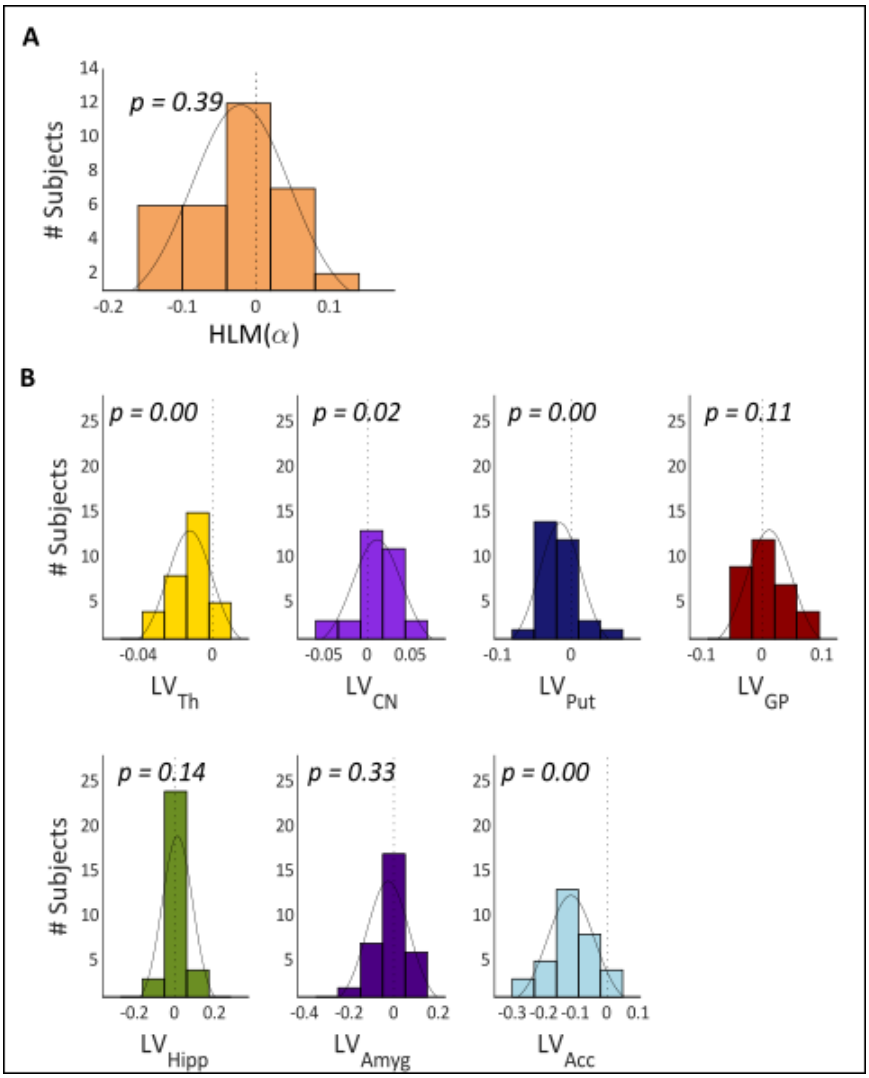

Figure 3. Hemispheric lateralization modulation (HLM(a)) grand average and basal ganglia volumes across all participants. A, The HLM(a) distribution across participants. While there was considerable variation across participants, we observed no hemispheric bias in lateralized modulation values across participants (p-value = 0.39). B, Histograms of the lateralization volumes of subcortical regions. We found that caudate nucleus was right lateralized (p-value = 0.021) whereas, putamen, nucleus accumbens and thalamus volumes showed left lateralization (p-value = 0.004, p-value < 0.001 and p-value < 0.001, respectively). Th = Thalamus, CN = Caudate nucleus, Put = Putamen, GP = Globus Pallidus, Hipp = Hippocampus, Amyg = Amygdala, Acc = Nucleus Accumbens.

Relationship between subcortical regions and hemispheric alpha lateralization

To test whether the individual hemispheric asymmetries in subcortical grey matter relate to variability in HLM(α), we subjected the MEG and MRI data to a General Linear Model (GLM). In this model, the individual HLM(α) values was the dependent variable, and the individual hemispheric lateralization volumes (LV) of the subcortical region were the explanatory variables. To discover the best set of subcortical structures that predict HLM(α) we used all possible combinations of regressors (LV) and selected the winning model based on lowest Akaike Information Criterion (AIC) scores. The winning model constituted of thalamus, caudate nucleus and globus pallidus and is defined as:

$$HLM(\alpha) \sim \beta_0 + \beta_1 LV_{Th} + \beta_2 LV_{CN} + \beta_3 LV_{GP} + \varepsilon$$

Where HLM(a) indicates the hemispheric lateralization modulation of alpha power and LV_{Th}, LV_{CN}, LV_{GP} refer to the lateralization volumes of thalamus, caudate nucleus and globus pallidus, respectively.

The analysis showed that the participants with larger volumes of the caudate nucleus in the left compared to the right hemisphere showed higher modulations in alpha power over the left compared to the right hemisphere (and vice versa). There was a trend for the same effect for the globus pallidus whereas the thalamus shows the opposite effect. These results were observed from the winning model that contained LV_{Th}, (beta = -2.19, $T_{(29)}$ = -2.74, se = 0.80, p = 0.010), LV_{CN} (beta = 0.92, $T_{(29)}$ = 2.83, se = 0.33, p-value = 0.008) and LV_{GP} (beta = 0.51, $T_{(29)}$ = 1.95, se = 0.26, p-value = 0.061) as regressors. This model predicted the HLM(α) values significantly in the GLM ($F_{3,29}$ = 7.4824, p = 0.0007, adjusted R^2 = .376) as compared with a null model (Figure 4A). These findings are illustrated in Figure 4B, confirming that both thalamus and caudate nucleus showed a significant linear partial regression with hemispheric lateralization modulation in the alpha band in the opposite and same direction. Although, the

beta estimate of LV_{GP} only showed a positive trend, removing it from the regression resulted in worse models (AIC table in supplementary material).

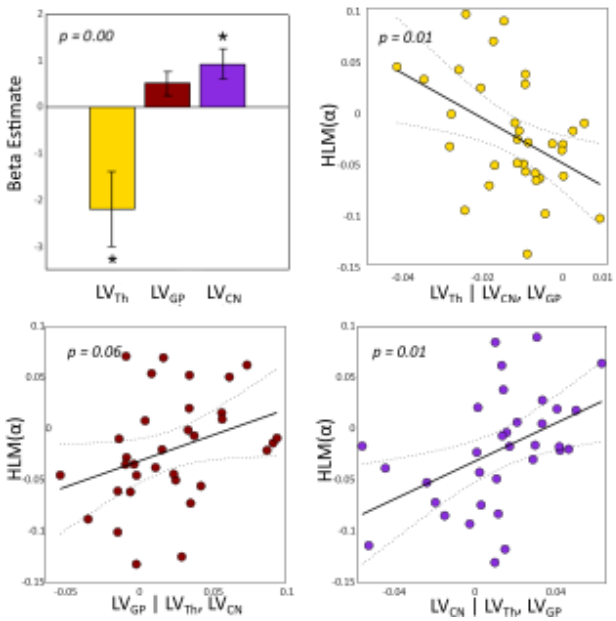

Figure 4. Lateralization volume of thalamus, caudate nucleus and globus pallidus in relation to hemispheric lateralization modulation of alpha (HLM(α)) in the task. A, The beta coefficients for the best model (containing three regressors) associated with a generalized linear model (GLM) where lateralization volume (LV) values were defined as explanatory variables for HLM(α). The model significantly explained the HLM(α) (p-value = 0.0007). Error bars indicate standard errors of mean (SEM). Asterisks denote statistical significance; *p<0.05. B, Partial regression plot showing the association between LV_{Th} and HLM(α) while controlling for LV_{GP} and LV_{CN} (p-value = 0.01). B, Partial regression plot showing the association between LV_{CN} and HLM(α) while controlling for LV_{Th} and LV_{GP} (p-value = 0.008). D, Partial regression plot showing the association between LV_{GP} and HLM(α) while controlling for LV_{Th} and LV_{CN} (p-value = 0.061) . Negative (or positive) LVs indices denote greater left (or right) volume for a given substructure; similarly negative HLM(α) values indicate stronger modulation of alpha power in the left compared with

the right hemisphere, and vice versa. The dotted curves in B, C, and D indicate 95% confidence bounds for the regression line fitted on the plot in red.

It is worth noting that neither the behavioural nor the rapid frequency tagging measures showed significant relationships with LVs and HLM(α).

Association between volumetric lateralization of subcortical regions and attention related to perceptual load conditions.

To relate load and salience conditions of the task to the relationship between subcortical structures and the alpha activity, we combined low-load or high-load targets with high-saliency or low-saliency distractors to manipulate the perceptual load appointed to each trial (Method section).

We therefore applied a multivariate multiple regression (MMR) using the HLM(α) values from each load/salience condition, and the LV values of the thalamus, caudate nucleus and globus pallidus (Equation 5). Comparison of the full (i.e., MMR including the LV values of all seven subcortical structures as regressors) and reduced (i.e., MMR with all structures excluding the selected structures) models showed that our selected regressors predicted variability in HLM(α) values to an extent that was greater than chance ($F_{(25,28)}$ = 2.03, p-value = 0.037). This was further confirmed when we compared the MMR model with the null model (i.e., MMR including only subject intercepts as regressor) ($F_{(29,31)}$ = 3.78, p-value = 0.0015). We next examined the extent to which LV values from each subcortical region predicted HLM(α) values for each load/salience condition. Our analysis, as shown in Figure 5, demonstrated that the thalamus had significant LV values in condition 1 (i.e., low-load target, non-salient distractor) with beta = -3.63 ($T_{(29)}$ = -2.64, se = 1.37, p-value = 0.0132). Globus pallidus showed a significant beta coefficient in conditions 2 (i.e., high-load target, non-salient distractor) and 3 (i.e., low-load target, salient distractor) with beta = 0.93, ($T_{(29)}$ = 2.15, se = 0.43, p-value = 0.040) and beta = 0.89 ($T_{(29)}$ = 2.30, se = 0.39, p-value = 0.029), respectively. Condition 4 (i.e., high-load target, salient distractor) was the only condition in which the caudate nucleus had a beta estimate significantly different than zero (beta = 1.64, $T_{(29)}$ = 2.07, se = 0.79, p-value = 0.049) . In sum,

this demonstrates that when the task is easiest (condition 1), the thalamus is related to alpha modulation. When the task is most difficult (condition 4), the caudate nucleus relates to the alpha modulation. For the conditions with medium difficulty (conditions 2 and 3) the globus pallidus related to the alpha band modulation.

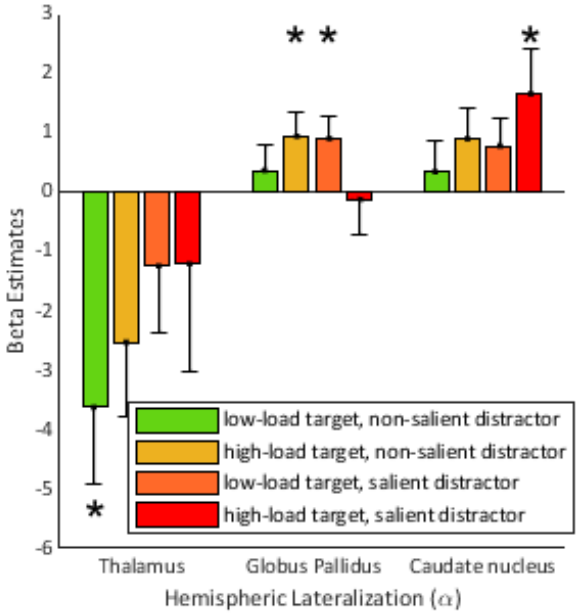

Figure 5. Beta estimates of subcortical nuclei from a multivariate regression model predicting HLM(α) in the four perceptual load conditions. Here the HLM(α) values for the four load conditions are the dependent variables and the lateralization volume of subcortical structures are the explanatory variables. The model significantly explains HLM(α) variability (p-value = 0.001) in comparison with null model). Error bars indicate SEM. Asterisks denote statistical significance; *p-value < 0.05.

Discussion

In the current study, we sought to identify the association between the volumetric hemispheric asymmetries in subcortical structures and the hemispheric laterality in the modulation of

posterior alpha oscillations during varying conditions of perceptual load. This association was tested in the context of a spatial attention paradigm where target load and distractor salience were manipulated. Our study resulted in two main findings: 1) globus pallidus, caudate nucleus, and thalamus predicted attention-related modulations of posterior alpha oscillations. 2) Each of these subcortical structures contributed differently to the lateralization values associated with the perceptual load conditions. For the easier task condition, the thalamus showed strong predictive power for alpha power modulation, whereas for mid-levels of load and salience, the globus pallidus showed predictive value. For the most perceptual demanding condition, we found that asymmetry of the caudate nucleus predicted alpha power modulation. These results shed light on the role of subcortical structures and their involvement in the modulation of oscillatory activity during the allocation of spatial attention.

Thalamus, Caudate nucleus, and Globus Pallidus are involved in the allocation of spatial attention.

While some MEG studies have demonstrated that it is possible to detect activity from deep structures such as the hippocampus (33–36), it is questionable whether one in general can use MEG to reliably detect activity from the thalamus and basal ganglia, owing to low SNR from sources close to the centre of the head (Baillet, 2017). Given these constraints, we instead correlated MEG data with structural magnetic resonance images to uncover functional contributions of subcortical structures to spatial attention.

We evaluated the relationship between subcortical structures and cortical oscillatory activity relying on the association between structure and function. Previous research points to a link between the volume of a given brain region and its functionality. For instance, it is well established that shrinkage (atrophy) in specific regions is a predictor of a number of neurological and psychiatric conditions including Parkinson's disease, dementia, and Huntington's disease. In Parkinson's disease, atrophy in the nucleus accumbens and thalamus correlated with cognitive impairments (39). In a large-scale study on 773 participants, patients with Alzheimer's Disease have been shown to have a significantly smaller amygdala, thalamus,

caudate nucleus, putamen, and nucleus accumbens than matched controls (40). Patients with symptomatic Huntington's Disease also show significantly smaller caudate nucleus than pre-symptomatic participants who were carriers of Huntington's Disease gene mutation (41).

Based on these considerations, we argue that the volume of basal ganglia relates to the ability to modulate posterior brain oscillations in attention type tasks. We demonstrated this by considering the hemispheric lateralization of the basal ganglia structures in relation to the ability to modulate posterior alpha oscillations. Using hemispheric lateralization circumvents the problem of how to account for individual differences in head-size. Our findings are consistent with previous studies suggesting that thalamic and basal ganglia structures are involved in modulating oscillatory activity in the alpha band. For example, the largest nucleus of the thalamus, the pulvinar, supports the allocation of spatial attention by driving the oscillatory synchrony in the alpha band between cortical areas in a task-dependent manner (42) Also, our finding are consistent with other studies suggestions a role for the caudate nucleus (43) and the pulvinar when allocating spatial attention (43–45). Stimulation of the subthalamic nucleus has been shown to suppress oscillatory activity in the alpha and beta (8-22Hz) frequency bands (46). Moreover, Mazzetti et al. (28) demonstrated a correlation between globus pallidus and lateralized modulation of alpha oscillation when spatial attention was modulated by reward outcomes.

Thalamus, Globus Pallidus, and Caudate nucleus play different roles in various load conditions.

Our results demonstrate a shift in the contribution of the thalamus, globus pallidus, and caudate nucleus when increasing the perceptual load of the target and saliency of the distractor. While in the low load, low saliency condition, the lateralized volume of the thalamus was correlated with the interhemispheric bias in alpha modulation, in the low load, high saliency, as well as high load, low saliency conditions, globus pallidus was related to the alpha oscillatory activity. Finally, the caudate nucleus was mainly associated with the high load, high saliency condition.

This differing pattern of the thalamic and basal ganglia structures might be suggestive of their respective contributions to the control of attentional resources. Involvement of the thalamus when the task is in its simplest form can be explained by its role relaying information between the basal ganglia and the prefrontal cortex (47,48). The involvement of the caudate nucleus in the most difficult condition is also in line with previous findings showing activation of caudate nucleus only in the higher-level cognitive hierarchy in a working memory selection (49) as well as a language task (48). The engagement of globus pallidus might be reflected from its central role in harmonizing firing rates across the cortico-basal-ganglia circuits (50). Globus pallidus also has wide projections to the thalamus (51) and can thereby impact the dorsal attentional networks by modulating prefrontal activities (11). Finally, our results on the globus pallidus are well aligned with the finding of Mazzetti et al. (28) also finding correlation between hemispheric lateralization of the globus pallidus and alpha oscillations in a spatial attention task.

Limitations and future directions

In the current study, we correlated the volumetric asymmetry of subcortical structures with the lateralized power of alpha oscillation. While this method provides novel insights into the role of subcortical structures in the modulation of oscillatory activity, it is indirect. The association between the function of subcortical nuclei and cortical oscillatory activity needs to be investigated further in electrophysiological studies that record the activity of both regions simultaneously. This could be done in non-human primates or in humans implanted with electrodes in the globus pallidus in treatment for Parkinson's Disease. In particular, EEG paired with globus pallidus recordings in participants performing spatial attention tasks would be of great value.

Moreover, our failure to identify a relationship between the lateralized volume of subcortical structures and behavioural measures could be addressed in studies that are better designed to capture performance asymmetries (52). Individual preferences toward one hemifield could potentially strengthen the power to detect correlations between structural variations in the

subcortical structures and behavioural measures. For example, it would be of great significance to investigate the lateralization of subcortical structures in patients with hemineglect in relation to right hemisphere lesions (53).

We did not show any association between the power of rapid frequency tagging signal and the size asymmetry of subcortical structures. As such there is an interesting dissociation between how alpha oscillations and neuronal excitability indexed by rapid frequency tagging relate to the involvement of subcortical structures. In previous work we have demonstrated that the attention modulation of the rapid frequency tagging signal is strongest observed in early visual cortex, whereas alpha oscillations are more strongly modulated around the parieto-occipital sulcus (54). It has been proposed that the modulation in rapid frequency tagging in early visual cortex with attention reflects gain control. According to this framework, we conclude that subcortical regions might not be involved in gain modulation in early visual cortex during the allocation of spatial attention, but rather in the downstream gating of visual information.

Conclusion

Our findings point to a link between thalamus and nuclei of the basal ganglia and measures of alpha oscillations in relation to spatial attention. Moreover, they demonstrate distinguished contributions of the different subcortical structures depending on target load or distractor salience, thus informing theories of how subcortical structures relate to oscillatory dynamics in challenging attentional settings. The stage is now set for further investigating the relationship between subcortical regions and the modulation of oscillatory activity. Linking brain oscillations to changes in subcortical regions associated with neurological disorders, such as Alzheimer's Disease (40,55) and Parkinson's Disease (Mak et al., 2014), could have potential clinical applications in terms of early diagnosis. Our approach could also be extended to other tasks resulting in hemispheric lateralization of oscillatory brain activity, e.g. working memory tasks (56) or language tasks (57). Our results also call for more direct investigations of the relationship between subcortical regions and neocortical oscillations which is best done by

intracranial recordings in non-human primates or utilizing human recording from deep-brain stimulation electrodes combined with EEG or MEG.

Methods and Materials

Participants

We analysed a previously collected dataset, described in (27). 35 right-handed healthy volunteers (25 female, mean age: 24 $\pm$ 5.7) participated. All reported normal or corrected-to-normal vision. One participant did not give consent for their data to be used outside of the original study and one was removed due to poor MRI [segmentation] quality, resulting in 33 participants in total. All subjects signed an informed consent form before participation and were paid £15 per hour. The study was conducted in compliance with the Declaration of Helsinki and was approved by the Science, Technology, Engineering, and Mathematics (STEM) ethical review committee of the University of Birmingham.

Experimental design

Participants were instructed to perform a cued change detection task (2 blocks of 256 trials, 45 minutes; Fig 1A), designed to assess selective attention function under varying conditions of perceptual challenge. Each trial started with a fixation point (1000ms) followed by two faces presented on the left and right side of the screen (1000ms). The fixation cross then turned into an arrowhead for 350ms cueing the left or the right hemifield. After a variable 1000 to 2000ms delay, the eye-gaze of each face randomly shifted rightward or leftward in a 150 ms interval. Then followed a 1000 ms response interval where participants were asked to respond with their right or left index finger whether the gaze direction shifted left or right (NAtA technologies, Coquitlam, BC, Canada). The experimental paradigm was implemented on a Windows 10 computer running MATLAB (Mathworks Inc., Natrick, USA) using Psychophysics Toolbox 3.0.11 (58,59).

Visual stimuli

Stimuli were circular faces that comprised 8˚ visual angle in diameter and placed with 7˚ eccentricity from fixation and were presented in the lower hemifield. Over trials, the perceptual load of targets was manipulated using a noise mask; masked targets are harder to detect and therefore incur greater cognitive load in their detection. The saliency of distractor stimuli was also manipulated using a noise mask; masked distractor stimuli are less salient and therefore less disruptive to performance on the detection task. The noise mask was created by randomly swapping 50% of the stimulus pixels (Figure 1B). This manipulation resulted in four target-load/distractor-saliency conditions: (1) target: low load, distractor: low saliency (i.e., clear target, noisy distractor), (2) target: high load, distractor: low saliency (i.e., noisy target, noisy distractor), (3) target: low load, distractor: high saliency (i.e., clear target, clear distractor), (4) target: high load, distractor: high saliency (i.e., noisy target, clear distractor) (Figure 1B and C). The stimulus set consisted of eight different face identities that were randomized across trials. On each trial, the identities of both stimuli were the same; however, to avoid visual differences between left and right the faces were mirror symmetric from the fixation point. Stimuli were projected using a VPixx PROPixx projector (VPixx technologies, Saint-Bruno, Canada) in Quad RGB mode (1440Hz) with an effective resolution of 960x540 pixels. Face stimuli were tagged with an invisible rapid-frequency-tagged flicker (for more details please refer to Gutteling et al., 2022). The distance between the participant and the projection screen was 148cm resulting in a 25.6˚ of visual angle screen.

Structural data acquisition

T1-weighted magnetic resonance images were acquired for 10 participants on a 3 Tesla Magnetom Prisma whole-body scanner (Siemens AG) with acquisition parameters: TR/TE = 2000/2.01 ms, TI = 880 ms, FoV = 256×256×208 mm^3, acquired voxel size = 1x1x1 mm^3. For 23 participants MRI images were attained from previous studies. These scans were obtained at the former Birmingham University Imaging Center (3-Tesla Philips Achieva Scanner: TR/TE = 7.4/3.5

ms, FA = 7°, FOV = 256x256x176 mm^3, acquired voxel size = 1x1x1 mm^3) were used. The 2 remaining participants provided their MRIs from other sources.

Structural data analysis

To segment the subcortical structures, FMRIB's Integrated Registration and Segmentation Tool (FIRST) v5.0.9 (www.fmrib.ox.ac.uk/fsl/, Oxford Centre for Functional MRI of the Brain) was used. FIRST is an automated model-based tool that runs a two-stage affine transformation to MNI152 space, to achieve a robust pre-alignment of the subcortical areas based on individual's T1-weighted MR images. Subcortical structures are modelled within a Bayesian framework (using manually segmented images provided by the Centre for Morphometric Analysis, CMA, MGH, Boston, as a prior) as surface meshes (masks) that were then fit to the registered image. Regions outside of the masks were excluded from subcortical alignment (60).

To assess hemispheric laterality for each SGM nucleus, we calculated the Lateralization Volume indices (LVs):

$$LV_s = \frac{V_{s_{right}} - V_{s_{left}}}{V_{s_{right}} + V_{s_{left}}} \qquad \text{Equation 1}$$

Where $V_{s_{right}}$ and $V_{s_{left}}$ represent the anatomical volume of a given subcortical structure (s) in number of voxels, in the right and left hemisphere, respectively. This equation implicitly controls for individual differences in brain volumes and has been commonly used to compute hemispheric structural asymmetries (Mazzetti et al., 2019). LVs can range between -1 and 1 where a positive LV indicates rightward asymmetry and vice versa.

MEG data acquisition

Electromagnetic data were recorded from participants while seated in upright position, using a 306-sensor whole-head TRIUX system from MEGIN (MEGIN, Stockholm, Sweden) including 102 magnetometers and 204 (2x102 orthogonal) planar gradiometers. The MEG data were sampled

at 1000Hz, following an embedded anti-aliasing low-pass filter at 330 Hz and stored for offline analysis. Head position of the participants was monitored by coils placed on anatomical fiducials (nasion, left and right periauricular points), digitized using a Polhemus Fastrack electromagnetic digitizer system (Polhemus Inc.). Eye movements were recorded using an Eyelink eyetracker (EyeLink 1000, SR research Ltd., Ottawa, Canada) along with vertical EOG sensors.

MEG data analysis

MEG data analysis was performed using custom scripts in MATLAB 2017a and 2019b (The MathWorks) and the FieldTrip toolbox (63). The analysis pipeline was adapted from the FLUX pipeline (64) and the scripts are available at https://github.com/tghafari/AMI_Substructures.

Preprocessing

Raw MEG data were high-pass filtered at 1Hz and demeaned. Then data were segmented in 4s epochs (-3s to 1s) relative to the target-onset (gaze shift of the face stimuli). Secondly, trials with sensors artifacts (e.g., jumps) were removed manually to prepare the data for automatic artifact attenuation using independent component analysis (ICA; "*runica.m*" in FieldTrip). Components related to eye blinks/movements, heartbeat and muscle activity were rejected. Thirdly, by visually inspecting the trials, we removed those containing clear residual artifacts such as eye blinks. We also removed trials with saccadic deviations larger than 3˚ from fixation (using EyeLink eye tracker data) during the 1.5s interval before target-onset (-1.5 – 0 s) (average ± SD = 13.7% ± 8.0 trials). Sensors that were removed during preprocessing were interpolated using a weighted neighbour estimate.

Time-frequency analysis of power

To calculate the time frequency representations (TFR) of power, we used a 3-cycle fixed time-window (e.g., 300ms for 10Hz) at each 10ms step. The data segments were multiplied by a Hanning taper to control the frequency smoothing and reduce spectral leakage. For

computational efficiency, we also used a zero-padding, rounding up the length of segments to the next power of 2. Then a fast Fourier transform (FFT) was applied to the tapered segments in the 2-30 Hz frequency range in 1Hz steps and the power was estimated. The power was then summed for each gradiometer pair.

To quantify the anticipatory oscillatory activity, we focussed on the -850 to 0 ms interval before target onset. To select sensors constituting the region of interest (ROI), we calculated the 8-13 Hz alpha modulation index (MI(a)) for all sensors. TFR of power for each sensor was averaged over all trials in the -850 to 0 ms interval, for attention to right and left. Then the MI(α) for each participant and each sensor was calculated as:

$$MI(\alpha)_k = \frac{Power(\alpha)_{k_{att\ right}} - Power(\alpha)_{k_{att\ left}}}{Power(\alpha)_{k_{att\ right}} + Power(\alpha)_{k_{att\ left}}} \qquad \text{Equation 2}$$

Where Power(α)$_k$ denotes the alpha power at sensor *k* in each condition.

Subsequently, at the group level, MI(α) for all sensors on the left hemisphere were subtracted from the corresponding sensors on the right hemisphere. The resulting values were then sorted and the five pair of sensors (n_{ROI}) that showed the highest difference in MI(a) values were selected, resulting in 10 sensors, symmetrically distributed over the right and left hemispheres.

To evaluate hemisphere-specific lateralization of alpha band modulation, we applied the hemispheric lateralization modulation (HLM(α)) index:

$$HLM(\alpha) = \frac{1}{n_{ROI}} \sum_{k=1}^{n_{ROI}} MI(\alpha)_{k_{right}} + \frac{1}{n_{ROI}} \sum_{k=1}^{n_{ROI}} MI(\alpha)_{k_{left}} \qquad \text{Equation 3}$$

Where n_{ROI} = 5 represents the number of sensors in each ROI and $MI(\alpha)_{k_{right}}$ or $MI(\alpha)_{k_{left}}$ denote the modulation index for sensor *k* over the right or left hemisphere, respectively.

Statistical analysis

Generalized Linear Model

To model how the mean expected value of HLM(α) indices depends on the lateralized volume of subcortical structures, we applied a generalized linear model (GLM) using HLM(α) values as the dependent variable and LV indices of subcortical structures as the systematic (explanatory) variables. We performed a collinearity analysis (*vif.m* function in MATLAB) to ensure that the predictor variables were sufficiently independent prior to performing the GLM analysis.

First, we sought to determine the best set of regressors that predicted variability in HLM(α) values. We therefore used all possible combinations of regressors (LVs; one to seven combinations) in a linear mixed-effects model (*fitme.m* function in MATLAB) to predict HLM(a) indices and selected the model that scored the lowest using the Akaike information criterion (AIC; (65)) score as the winning model. We confirmed our findings using Bayesian information criterion (BIC; (66)) and produced similar results. These values are commonly used to identify the best point of trade-off between fit and model complexity.

To estimate the beta weights of the winning model the optimal set of regressors (here LV_{Th}, LV_{CN} and LV_{GP}) were used as the explanatory variables in a GLM (*fitlm.m* function in MATLAB) to predict HLM(a) values with the following formula:

$$HLM(\alpha) \sim \beta_0 + \beta_1 LV_{Th} + \beta_2 LV_{CN} + \beta_3 LV_{GP} + \varepsilon \qquad \text{Equation 4}$$

Here, LV_{Th}, LV_{CN} and LV_{GP} refer to the lateralization volume of thalamus, caudate nucleus, and globus pallidus, respectively.

Multivariate multiple regression

To simultaneously model the predictive relationship between the lateralized volume of thalamus, caudate, and globus pallidus, and all four load conditions, we used a multivariate multiple regression (MMR) (67) analysis. MMR is used to predict multiple dependent variables

using multiple systematic parameters. It allows for modifying our hypothesis tests and confidence intervals for explanatory parameters and responses, respectively (68). The model was defined as:

$$HLM(\alpha_1) + HLM(\alpha_2) + HLM(\alpha_3) + HLM(\alpha_4) \sim \beta_0 + \beta_1 LV_{Th} + \beta_2 LV_{CN} + \beta_3 LV_{GP} + \varepsilon$$

Equation 5

Where HLM(α) refers to hemispheric lateralization modulation of alpha power in load conditions 1 to 4 (Figure 1C), respectively; β refers to the coefficients in the model; LV_{Th}, LV_{CN} and LV_{GP} refer to the lateralization volume of thalamus, caudate nucleus, and globus pallidus, respectively.

To ensure our chosen MMR predicts meaningful variance in HLM(a) scores, we compared a full model containing LV indexes from all 7 subcortical regions to one where the key structures of interest (i.e., thalamus, caudate nucleus, and globus pallidus) had been removed, leaving putamen, nucleus accumbens, hippocampus, and amygdala as regressors. This model is referred to as the reduced model. We also compared a model containing the key regressors of interest (LV_{Th}, LV_{CN}, LV_{GP}) to a null model that contained only subject intercepts as regressors. Models were compared one-way ANOVA test in RStudio (version 2022.02.0) (69).

Behavioral data analysis

To evaluate if the participants response times and accuracy was correlated with the hemispheric lateralization of alpha oscillatory activity as well as lateralized volume of subcortical structures, we calculated behavioral asymmetry (BA) as below:

$$BA_{ACC/RT} = \frac{ACC/RT_{att\ right} - ACC/RT_{att\ left}}{ACC/RT_{att\ right} + ACC/RT_{att\ left}}$$

Equation 6

Where $ACC/RT_{att\ right}$ and $ACC/RT_{att\ left}$ correspond to the behavioural asymmetric performance in accuracy or response times when the attention was toward right or left visual hemifield, respectively. We then calculated the Pearson correlation between the BA and HLM.

Finally, we ran the winning GLM model with accuracy and response times as the dependent variable and LV_{Th}, LV_{CN}, and LV_{GP} as the regressors.

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