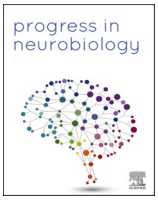
Progress in Neurobiology 226 (2023) 102466

Contents lists available at ScienceDirect

Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio



Causal manipulation of gaze-following in the macaque temporal cortex

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ARTICLE INFO

Keywords:
Gaze-following patch
Joint attention
Microstimulation
Muscimol inactivation
Superior temporal sulcus
Social interaction

ABSTRACT

Gaze-following, the ability to shift one's own attention to places or objects others are looking at, is essential for social interactions. Single unit recordings from the monkey cortex and neuroimaging work on the human and monkey brain suggest that a distinct region in the temporal cortex, the gaze-following patch (GFP), underpins this ability. Since previous studies of the GFP have relied on correlational techniques, it remains unclear whether gaze-following related activity in the GFP indicates a causal role rather than being just a reverberation of behaviorally relevant information produced elsewhere. To answer this question, we applied focal electrical and pharmacological perturbation to the GFP. Both approaches, when applied to the GFP, disrupted gaze-following if the monkeys had been instructed to follow gaze, along with the ability to suppress it if vetoed by the context. Hence the GFP is necessary for gaze-following as well as its cognitive control.

1. Introduction

Gaze-following involves extracting directional information provided by the other's eyes, head or body orientation and using this information to redirect one's own attention to the same location or object that has attracted the other's attention, i.e. to establish "joint attention" (Emery, 2000). As joint attention allows us to map our own object-associated intentions and aspirations onto the other, it facilitates our ability to establish fruitful interactions. Gaze-following is not confined to humans, but has been demonstrated in many nonhuman primates (Tomasello et al., 1998; Emery et al., 1997; Burkart and Heschl, 2006; Marciniak et al., 2015; Spadacenta et al., 2019) as well as some other animals (Bräuer et al., 2004; Bugnyar et al., 2004; Kaminski et al., 2005; Wilkinson et al., 2010; Simpson and O'Hara, 2019). Gaze-following of macaques, arguably the best studied nonhuman primate species, shares many similarities with human gaze-following, which include precision, reflexivity, and the possibility for it to occur overtly or covertly (Marciniak et al., 2015; Deaner and Platt, 2003).

Previous fMRI experiments on humans and monkeys, as well as electrophysiological studies of the monkey brain concur that a distinct region in the posterior part of the temporal cortex, the "gaze-following patch (GFP)", is specifically involved in converting directional information on the other's gaze direction into precise spatial signals that redirect the observer's focus of attention (in humans (Kraemer et al., 2020; Marquardt et al., 2017; Materna et al., 2008; Pelphrey et al., 2003), in monkeys (Kamphuis et al., 2009; Marciniak et al., 2014; Ramezanpour and Thier, 2020; Ramezanpour et al., 2021). More specifically, the single unit recordings from the monkey GFP indicate that GFP neurons link information on the other's gaze direction with distinct targets flexibly, in a manner that may also allow the executive control of gaze-following (Ramezanpour and Thier, 2020). However, causal evidence for this is still lacking as previous studies of experimental or clinical lesions of parts of the temporal lobe lacked the necessary anatomical and functional specificity. For instance, the latter characterizes a clinical case study of a patient exhibiting a gaze-following deficit due to a large and poorly delineated lesion of her right superior temporal gyrus resulting from hemorrhage (Akiyama et al., 2006a). In this same patient, and also in others who underwent anterior temporal lobectomy, the ability to use the other's gaze to reflexively and covertly shift attention was deteriorated (Akiyama et al., 2006b; Okada et al., 2008). Already earlier it had been shown that macaque monkeys with their rostral STS removed bilaterally had difficulty in differentiating direct from averted gaze (Campbell et al., 1990). More recently, it was shown that reversible lesions of face patches in the macaque posterior STS compromised reflexive head-gaze following (Roy et al., 2014). However, in this case gaze-following was only indirectly assessed by saccade target choices in a discrimination task, with the other's gaze serving as a distractor. Considering the well-established role of the

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https://doi.org/10.1016/j.pneurobio.2023.102466
Received 23 December 2022; Received in revised form 9 May 2023; Accepted 17 May 2023
Available online 20 May 2023

temporal lobe face patch system in processing head orientation (Freiwald and Tsao, 2010; Yang and Freiwald, 2021; Chang and Tsao, 2017; Taubert et al., 2020) and the lack of information on the spatial relationship of the lesions to the elements of this system and the GFP, the interpretation of the reported deficits remains ambiguous. Rather than reflecting an impairment of gaze-following due to an inability to use the other's gaze to establish joint attention, they might have been a consequence of a more elementary inability to extract pertinent information on head gaze.

Previous work on the monkey's face patch system has successfully deployed well targeted causal interference experiments to compromise the observer's ability to detect faces or extract information on particular aspects of faces such as identity (Sadagopan et al., 2017; Moeller et al., 2017). While these experiments were grounded in precise knowledge of the location of the face patch system, they did not target the GFP and apart from aiming at different locations, they did not involve the more elaborated behavioral paradigms needed to selectively probe gaze-following and its executive control, i.e. the ability of the observer to shift attention guided by the other's gaze if pertinent and to suppress it if inappropriate. Besides, the GFP does not harbor typical properties of a face patch, i.e. face selectivity (Marciniak et al., 2014; Ramezanpour and Thier, 2020), and therefore any attempts to explore gaze-following through the face patch system may have only indirectly and unknowingly involved the GFP. Hence, there is need to combine suitable behavioral paradigms with knowledge about the precise location of the GFP. In an attempt to meet these demands, we used two well established causal interference techniques, electrical microstimulation and muscimol injections, to reversibly perturb the GFP, identified on the basis of single unit responses, and to examine the consequences for gaze-following behavior. More specifically, we asked if disruption of the GFP could abolish the observer's linkage between an object and a conspecific gazing at it. The results obtained clearly indicate that the GFP acts as a gatekeeper that allows gaze-following if pertinent and vetoes it in case the given context might render gaze-following inappropriate.

2. Results

2.1. Behavioral paradigm

Our behavioral paradigm (Fig. 1) required the experimental monkeys to identify particular spatial targets relying on expedient information provided by the face and head of a conspecific displayed on a monitor in front of the observer. In the first condition, an instruction cue presented early in a trial told the observer to follow the conspecific's head gaze direction to one out of four possible spatial targets (henceforth referred to as the gaze-following task) by making a precise indicative saccade, while ignoring the fact that the identity of the demonstrator varied. We used head directions to drive gaze-following in our paradigm (as well as in our previous work) given the dominating view in the literature on nonhuman primates is that head orientations may be the primary source of information guiding the observer's attention (Tomasello et al., 2007; Kobayashi and Kohshima, 2001). As the eyes of the demonstrator were kept straight relative to the head, head direction equaled gaze direction and we refer to the observer's behavioral reaction as head gaze following or in short gaze-following.

In the second condition, identified by a different instruction cue, the observer had to ignore the demonstrator's gaze direction and select a spatial target, resorting to learned associations between four possible facial identities and the four targets (identity-mapping task). Previous work by Marciniak et al (Marciniak et al., 2014). has verified that the monkeys do not treat this gaze-following task as another learned association task like identity-mapping, and are able to compute the gaze vector of the portraits accordingly. This same behavioral paradigm was used by Ramezanpour and Thier (Ramezanpour and Thier, 2020) in their electrophysiological analysis of the GFP and neighboring parts of the superior temporal sulcus (STS). The experiments reported here employed the same monkeys whose right hemispheres had been explored in those studies. This allowed us to rely on available data on the coordinates of the GFP and neighboring elements of the face patch system. For electrical microstimulation we chose sites in the GFP and a control area located 4 millimeters anterior to the GFP (please refer to the Methods section for full details on the paradigm).

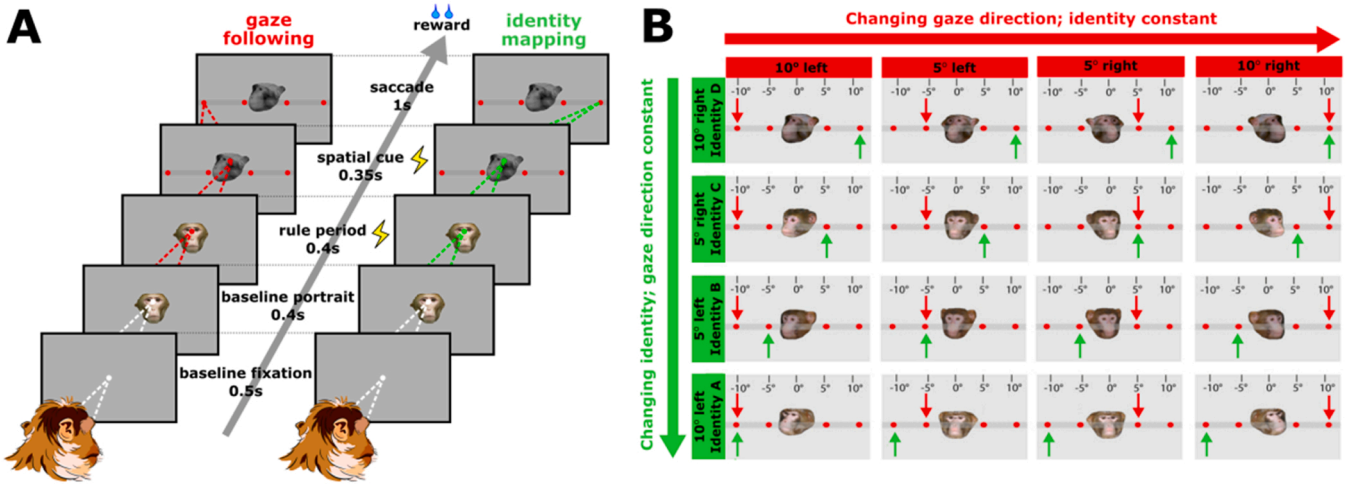

Fig. 1. Behavioral paradigm and microstimulation protocol. **A.** The experimental requirements involved a gaze-following and identity-mapping task, visually identical in every aspect apart from the instruction to shift attention towards spatial targets via the following of head gaze (red cue), or to select a target based on a learned association between the demonstrator's identity and distinct targets (green cue). Here we illustrate how a gaze-following (left) or identity-mapping (right) trial unfolds, beginning with a baseline period in which the observer fixates a central dot, continued fixation when a portrait appears, followed by presentation of the rule, represented by a change of the color of the fixation dot to either red (gaze-following) or green (identity-mapping), the turn of the demonstrator to one of the 4 targets (spatial cue period) and finally an indicative saccade to the target singled out by gaze or identity, depending on the rule, to be released upon the disappearance of the central fixation dot. Microstimulation was applied to either the rule period or the spatial cue period (marked with lightning bolts). **B.** Summary of the 16 combinations of 4 demonstrator portraits and the 4 possible gaze directions. Four identities (A-D) were involved in the paradigm, and each row represents the identity of the portrait used for identity-mapping (relevant target highlighted by green arrow). The demonstrator could gaze in four possible directions meeting one of the 4 targets at 10° left, 5° left, 5° right, or 10° right, (relevant target highlighted by red arrow). Gaze direction is kept constant along the matrix columns.

There were two windows of interest in our behavioral paradigm, the rule period and the spatial cue period (Fig. 1A). 500 ms after trial onset, a forward-oriented neutral monkey face appeared, centered behind a white fixation point. This neutral monkey face is a remnant of our previous attempts to localize (Marciniak et al., 2014) and characterize (Ramezanpour and Thier, 2020) the GFP in the macaque brain. For the purpose of consistency we have maintained the use of this neutral face in the baseline period. The instruction to follow gaze or, alternatively to map identities was provided by a change of color of the white fixation point (to red for gaze-following, to green for identity-mapping) 400 ms later. After another 400 ms, the neutral monkey face was replaced by the demonstrator monkey and four spatial targets, and the disappearance of the red/green fixation point 350 ms later served as a go cue for the experimental monkey to commence gaze-following or identity-mapping (Fig. 1B), depending on the prevailing rule.

Microstimulation afforded the necessary temporal resolution that allowed us to selectively manipulate information processing in the two windows of interest, first the period in which the demonstrator turned his gaze to a particular target (spatial cue period) and second in the earlier period in which the rule in force in a trial (rule period) was provided (Fig. 1A). Electrical microstimulation was delivered to the region of choice in the right posterior STS (pSTS) in one of these two

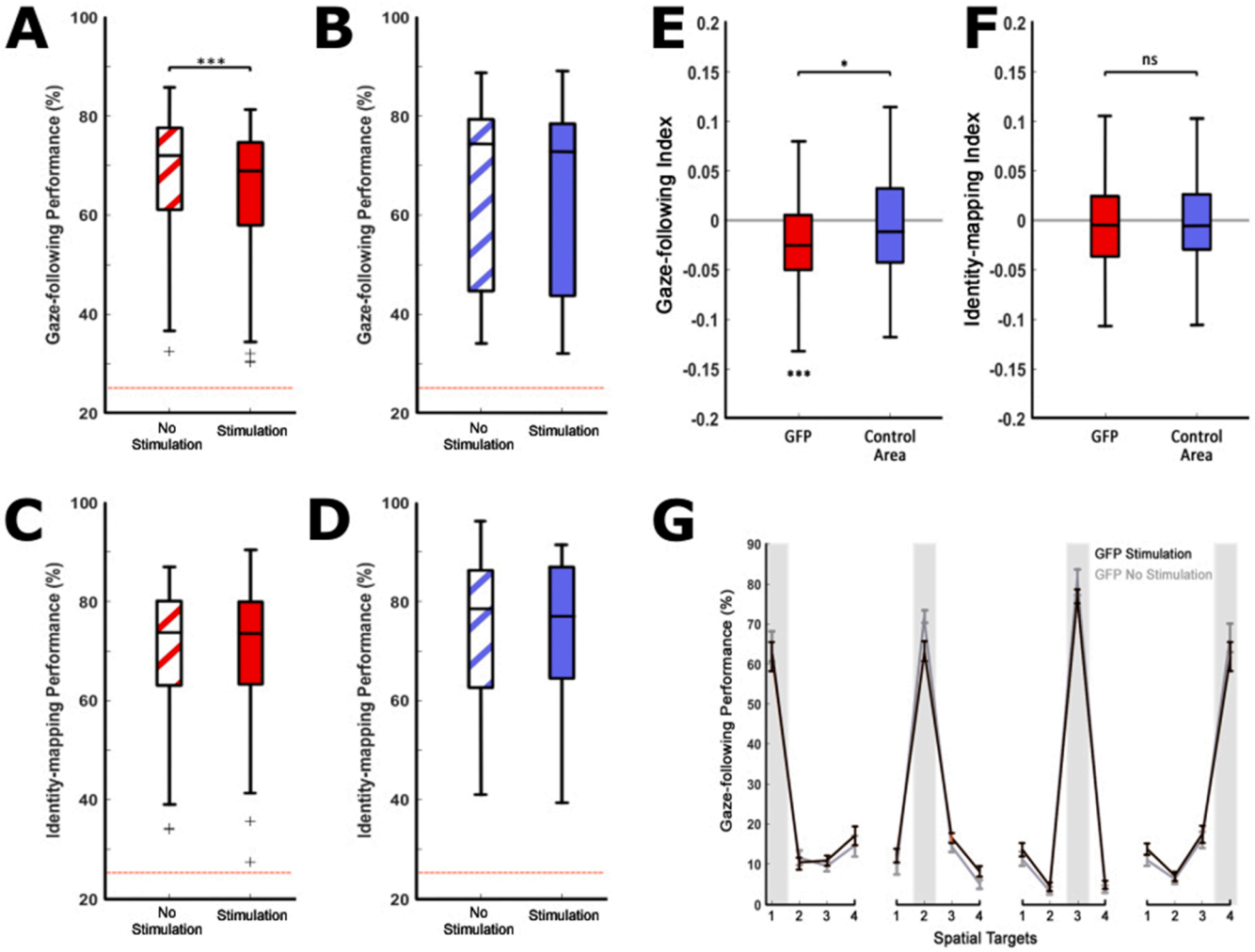

Fig. 2. The effect of electrical microstimulation on task performance when applied in the spatial cue/target window. **A, B.** Pooled gaze-following performance of 2 monkeys (127 sessions) when microstimulation was applied (solid boxes) to the GFP (65 sessions) (A) and control area (62 sessions) (B), compared to when no stimulation (striped boxes) was provided. Microstimulation significantly reduced gaze-following performance only when applied to the GFP. For Fig. 2A-F, the median is indicated by the solid black line within the box, and the whisker length is set at 1.5x the interquartile range. The horizontal red dashed line represents the chance level (25%) of the gaze-following paradigm. Black crosses represent 1.5x interquartile outliers. Wilcoxon signed-rank test was performed, *** $P < 0.001$. **C, D.** Pooled identity-mapping performance of 2 monkeys (127 sessions) when microstimulation (solid boxes) was applied to the GFP (65 sessions) (C) and control area (62 sessions) (D), compared to when no stimulation (striped boxes) was applied. Wilcoxon signed-rank test was performed, $p > 0.05$. **E.** Mean gaze-following index for sessions in which microstimulation was applied to the GFP (red) and the control area (blue). Only in the case of microstimulation of the GFP during gaze-following is the gaze-following index significantly different from zero, one sample Student's t-test, ** $P < 0.01$. Comparison of the gaze-following index between the GFP and the control area also exhibited a significant difference; Wilcoxon signed-rank test, * $P < 0.05$. **F.** Mean identity-mapping index for sessions in which microstimulation was delivered to the GFP (red) and the control area (blue). In neither the GFP nor the control area did microstimulation cause any change in the identity-mapping index. There was also no difference between the identity-mapping index of the GFP and the control area. **G.** Each line graph compares the gaze-following performance (y-axis) for each of the targets (x-axis), with respect to the correct spatial target. Peaks in each line graph (also highlighted by the grey mask) correspond to the gaze cued target, and reflect the monkeys' performance, i.e. greatest preference for Target 1 when the monkey was *meant* to be selecting Target 1. Grey and black lines represent unstimulated and stimulated conditions in the GFP respectively, and mean performance ± SEM for each target is shown. The spatial targets labeled 1–4 correspond to the 4 spatial targets 10° left, 5° left, 5° right, and 10° right respectively. While there are some small yet significant spatial biases in the false saccadic choices (grey), importantly these biases are unaffected by microstimulation of the GFP (black).

windows of interest per session, as described in greater detail in the methods section. A total of 127 sessions were completed (40 in Monkey T and 87 in Monkey L) for the spatial cue period, whilst 50 sessions were completed (in Monkey L) for the rule period.

2.2. Microstimulation of the GFP impairs gaze-following performance

For each experimental session, we separated the gaze-following and identity-mapping trials that had been presented randomly interleaved and examined how microstimulation affected task performance in these two conditions (see Supplementary Figures for separated monkey data). Fig. 2A and B compare the performance of gaze-following when stimulation was applied to the GFP and the control area during the spatial cue period against baseline performance, i.e. the behavior in the absence of stimulation, pooling data across the two monkeys. Microstimulation in the GFP significantly impaired the gaze-following performance (Fig. 2A, Wilcoxon signed-rank test, GFP: $p < 0.001$). The magnitude of performance change (3.2%) was comparable with the degree of disruption of other vision-dependent functions reported as a consequence of microstimulating other parts of the monkey temporal cortex (Afraz et al., 2006; Kawasaki and Sheinberg, 2008). The effect size of the microstimulation in the GFP for gaze-following was 0.4595 (Cohen's d), indicating a small to medium effect. It is possible that in a species lacking substantial hemispheric specialization, most probably the unstimulated left hemisphere accommodates a GFP, left untainted by microstimulation. Moreover, considering the current size used, microstimulation most probably affected only parts of the right GFP. In any case, no impairment of gaze-following was observed when the control area was stimulated (Wilcoxon signed-rank test, $p = 0.31$, Cohen's $d = 0.1381$). On the other hand, microstimulation of the GFP had no effect on the performance in the identity-mapping task (Fig. 2C and D; Wilcoxon signed-rank test, GFP: $p = 0.59$ and Control Area: $p = 0.71$, Cohen's $d = 0.0143$ and -0.0156 respectively). This is a clear demonstration that normal gaze-following requires the GFP. Moreover, the effect is specific to the GFP, as disruption of the neighboring control cortical area had no effect on gaze-following. Stimulation of neither the GFP nor the control area evoked changes in the latencies of the gaze-following or identity-mapping saccades. This may be a result of the use of a go cue in the paradigm that prevented the preemptive initiation of gaze-following or identity-mapping saccades.

We calculated a gaze-following and an identity-mapping index (see Methods) for the GFP and the control area to better understand the effects of microstimulation on these two cortical areas. A selectivity index tending towards 1 would indicate suppression in the respective task, whilst an index tending towards +1 would indicate that task performance had actually been enhanced by the perturbation. In Fig. 2E we show that there is a clear suppressive effect of microstimulating the GFP (one sample Student's t-test, $p < 0.001$), that is restricted to gaze-following (Wilcoxon signed-rank test, $p < 0.05$). Microstimulating the control area (gaze-following: $p = 0.31$, identity-mapping: $p = 0.59$) and microstimulating the GFP for identity-mapping ($p = 0.85$) (Fig. 2E and F) did not yield significant effects, affirming the specificity of the GFP in controlling gaze-following behavior.

2.3. Stimulation-evoked errors in gaze-following are neither a consequence of resorting to an identity-mapping strategy nor due to target bias

To further explore why microstimulation of the GFP disrupted gaze-following, we looked into the error trials in order to test two possibilities. First, microstimulation might have disturbed the monkey's ability to distinguish between the two tasks because of a stimulation-based bias for the identity-mapping task. Second, microstimulation might have induced a spatial bias, i.e. a preference for a particular target. The first possibility can be ruled out by asking if incorrect choices in gaze-following trials in which the GFP was stimulated would be interpreted as correct behavioral choices assuming that the monkeys had adopted an identity-mapping strategy, no matter that the rule required gaze-following. Given the complexity of our behavioral paradigm which required careful attention to the rule and then to apply the appropriate strategy, there is an inherent tendency to mistake gaze-following for identity-mapping, and vice versa. Therefore, what we would be assessing is whether or not perturbation of the GFP could further shift this bias towards one or the other task. However, we found that the behavioral decisions in gaze-following error trials did not exhibit a significant effect of identity on the target choices (Wilcoxon signed-rank test, GFP: $p = 0.36$). As stated before, stimulating the control area did not impair the overall performance in the gaze-following condition, and correspondingly there was also no significant change in the likelihood of rule misinterpretation (Control area: $p = 0.14$). In short, error trials produced under the effect of microstimulation could not be led back to the erroneous pursuit of an identity-mapping strategy in the presence of the gaze-following rule. Since perturbation of the GFP produced no impairment in identity-mapping, we did not expect any bias towards gaze-following. We found no significant change in error trials performed as gaze-following when identity-mapping was cued, neither in the GFP ($p = 0.33$) nor the control area ($p = 0.72$).

We next examined if the impairment of the gaze-following performance upon microstimulation of the GFP could be due to the introduction of a bias for particular targets, which we show in Fig. 2G. The pattern of false target choices exhibited subtle, yet significant spatial biases (Kruskal-Wallis ANOVA, Target 1 cued: $p < 0.05$, Target 2 cued: $p < 0.001$, Target 3 cued: $p < 0.001$, Target 4 cued: $p < 0.001$). However, the bias patterns were not consistent across the targets. For instance in case Target 2 was at stake, more false indicative saccades were made to neighboring Target 3, whereas in case the demonstrator's gaze was directed at Target 3 more false saccades were made to Target 1, i.e. the most distant target. Importantly, in no case were these highly idiosyncratic bias patterns affected by microstimulation (Wilcoxon signed-rank tests were not significant across all targets). Hence, the conclusion is that microstimulating the GFP in the spatial cue period, i.e. during shifts of attention guided by the other's gaze, evokes random shifts of attention. These random shifts could be a consequence of a compromised ability of GFP neurons to use gaze information to identify distinct spatial targets.

As said above, identity-mapping was unaffected when targeting the GFP with microstimulation in the spatial cue period (Fig. 2C). However, although the percentage of error trials did not change significantly, the basis of the errors was affected. This is indicated by the fact that the proportion of error trials that could be led back to the monkey selecting the target identified by the demonstrator's gaze direction dropped significantly (Wilcoxon signed-rank test, $p < 0.01$). This effect may suggest the working of a residual drive to follow gaze persisting during identity-mapping that is further reduced by microstimulation in the spatial cue period. Why then did the overall number of error trials stay the same, rather than decline? One may speculate that stimulation induced a compensatory increase in the number of unsystematic errors, also responsible for the drop in performance in the gaze-following condition. Stimulating the control area did not produce any bias in task preference when identity-mapping was underway ($p = 0.46$).

2.4. Microstimulation of the GFP during the rule presentation period spares gaze-following and instead compromises identity-mapping

We also had the opportunity to study the effects of microstimulation in the rule period of the paradigm in Monkey L. When we targeted this window of the paradigm, we no longer observed an impairment of gaze-following when stimulating the GFP (Fig. 3A; Wilcoxon signed-rank test: $p = 0.21$). Yet, stimulation of the GFP significantly impaired identity-mapping (Fig. 3B; $p = 0.0019$). These differential effects were apparently a consequence of a reduced impact of the identity-mapping strategy. This conclusion is suggested by the fact that interfering with the

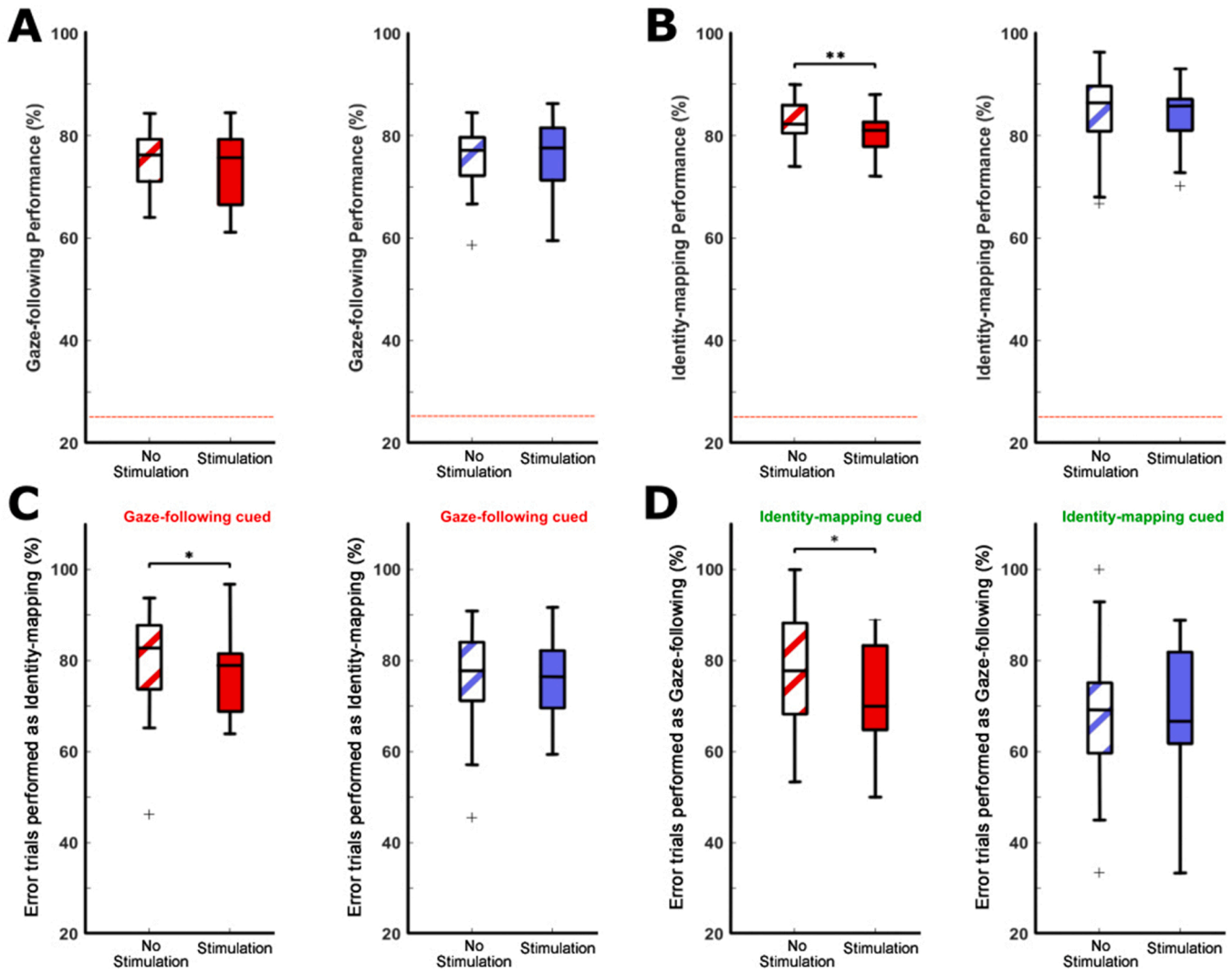

Fig. 3. Effect of microstimulation during rule presentation. **A.** Gaze-following performance of Monkey L (50 sessions) when microstimulation was applied to the GFP and control area (left and right boxplots respectively). For Fig. 3A-D, the median is indicated by the solid black line within the box, and the whisker length is set at 1.5x the interquartile range. The horizontal red dashed line represents the chance level (25%) of the gaze-following paradigm (A and B). Black crosses represent 1.5x interquartile outliers. **B.** Identity-mapping performance of Monkey L (50 sessions) when microstimulation was applied to the GFP and control area (left and right boxplots respectively). Microstimulation significantly reduced identity-mapping performance when applied to the GFP during the rule period of the behavioral paradigm (Wilcoxon signed-rank test, ** $P < 0.01$). **C.** In all error trials, there is a likelihood of an incorrect gaze-following trial to be performed as an identity-mapping trial. Here we compare how this tendency to resort specifically to identity-mapping may change when stimulation was targeted to the GFP and control area (left and right boxplots respectively). There is a significant decrease in the tendency to resort to identity-mapping (Wilcoxon signed-rank test, * $P < 0.05$) when the GFP is targeted with microstimulation during the rule period. **D.** Likelihood of an incorrect identity-mapping trial to be performed as a gaze-following trial when stimulation was targeted to the GFP and control area (left and right boxplots respectively). There is a significant decrease in the tendency to resort to gaze-following (Wilcoxon signed-rank test, * $P < 0.05$) when the GFP is targeted with microstimulation during the rule period.

activity of the GFP during the rule period window led to a significant decrease in false gaze-following decisions when actually identity-mapping had been required (Wilcoxon signed-rank test: $p < 0.05$, Fig. 3D). Moreover, the number of false identity-mapping decisions in trials in which gaze-following was demanded, decreased significantly (Wilcoxon signed-rank test: $p < 0.05$, Fig. 3C). Taken together, the results in Fig. 3C and D suggest that there is a reduced tendency to apply the incorrect rule. Importantly, the effects of microstimulation during the rule period were specific to the GFP as stimulation of the control area did not have an effect on performance, no matter what the task was (gaze-following: $p = 0.80$, identity-mapping: $p = 0.25$). Finally, no task bias was observed in the control area for either gaze-following ($p = 0.89$) or identity-mapping ($p = 0.99$).

2.5. Muscimol inactivation of the GFP strongly impairs gaze-following and can be led back to an identity-mapping strategy being employed

We complemented the microstimulation experiments in monkey L by reversibly deactivating the GFP and the control area with focal muscimol injections (14/44 and 7/44 sessions respectively), promising stronger effects, albeit at the expense of losing the temporal specificity afforded by microstimulation. The performance after the muscimol-based deactivation of the targeted tissue was compared against control sessions in which no injections (GFP: 7/44, control area: 7/44) or saline injections (GFP: 6/44, control area: 3/44 sessions) had been carried out. The individual muscimol volumes injected (2 – 2.8 μl at a concentration of 10 μg/μl) are known to silence neural activity in regions with a diameter of 1 – 3 mm (Roy et al., 2014; Sadagopan et al., 2017).

Indeed muscimol injections into the GFP caused a clear and highly

significant deterioration (15.24% decrease) of gaze-following that was substantially larger than the one evoked by microstimulation during the spatial cueing period (Fig. 4A, Wilcoxon rank-sum test, GFP: $p < 0.0001$, Cohen's $d = 2.8263$). On the other hand, muscimol inactivation of the control area did not have an effect on the monkey's ability to follow gaze ($p = 0.19$, Cohen's $d = -0.3509$). Finally, neither the inactivation of the GFP nor the control area had an effect on the identity-mapping performance (Fig. 4B, $p = 0.90$ and $p = 0.98$ respectively, Cohen's $d = -0.1407$ and 0.2757 respectively). Why do muscimol injections into the GFP compromise gaze-following? A closer look at the monkey's decision pattern clearly indicated that it was a consequence of the monkey mixing up rules. Rather than undergoing gaze-following when required, on error trials the monkey's choices reflected target selections guided by the demonstrator's identity resulting in a significantly increased number of false decisions determined by identity when compared to control sessions (Fig. 4C, left, Wilcoxon rank-sum test, GFP: $p = 0.008$). On the other hand, when identity-mapping was demanded, the monkey was committed to the task as indicated by the fact that the number of false gaze-following decisions did not change (Fig. 4D, left, GFP: $p = 0.22$).

Finally, injecting the control area did not affect the number of error trials no matter if gaze-following or identity mapping had been required (Fig. 4A and B, right). The proportion of errors attributable to identity-mapping during a gaze-following trial was not significantly different after inactivation of the control area (Fig. 4C, right, $p = 0.62$). In the same vein, the proportion of errors attributable to false decision to follow gaze during identity-mapping trials did not change (Fig. 4D, right, $p = 0.27$).

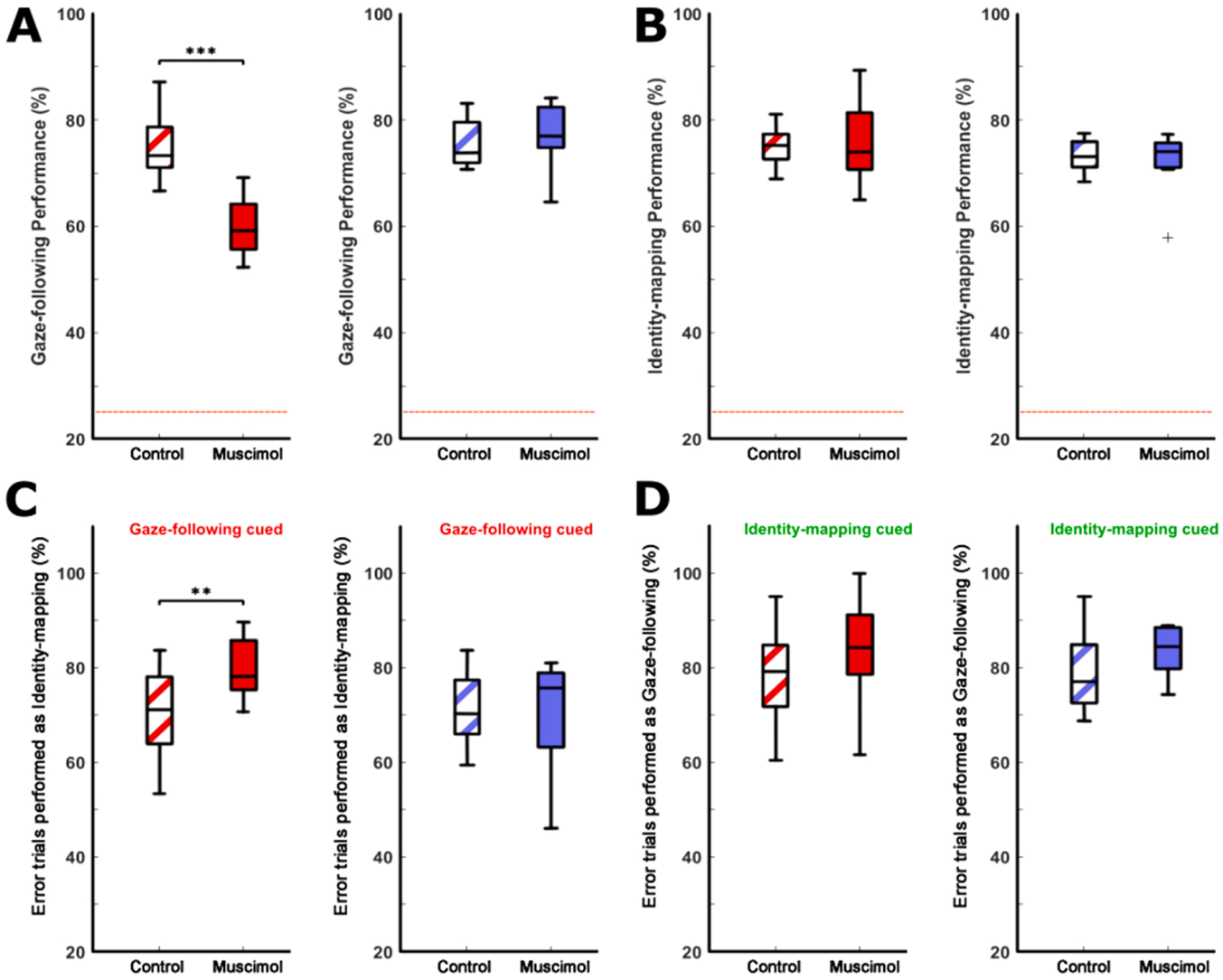

Fig. 4. Effect of muscimol inactivation in the GFP and control area on gaze-following and identity-mapping performance. **A.** Gaze-following performance of Monkey L when muscimol was injected into the GFP (14 sessions) and control area (7 sessions) (left and right boxplots respectively). Control injection conditions comprised of a combination of saline injections or sessions without injection (in total 13 control sessions in the GFP, 10 for the control area). For Fig. 4A-D, the median is indicated by the solid black line within the box, and the whisker length is set at 1.5x the interquartile range. The horizontal red dashed line represents the chance level (25%) of the gaze-following paradigm (A and B). Black crosses represent 1.5x interquartile outliers. Gaze-following performance is significantly impaired upon inactivation of the GFP; Wilcoxon signed-rank test, *** $P < 0.001$. **B.** Identity-mapping performance when muscimol was injected into the GFP and control area (left and right boxplots respectively). Wilcoxon signed-rank test, $p > 0.05$. **C.** In all error trials, there is a likelihood of an incorrect gaze-following trial to be performed as an identity-mapping trial. Here we compare how this tendency to resort specifically to identity-mapping may change when the GFP and control area were inactivated (left and right boxplots respectively). Wilcoxon signed-rank test: ** $P < 0.01$. There is a significant increase in the tendency to resort to identity-mapping upon inactivation of the GFP. **D.** Likelihood for an incorrect identity-mapping trial to be performed as a gaze-following trial when the GFP and control area were inactivated (left and right boxplots respectively). Wilcoxon signed-rank test, $p > 0.05$.

3. Discussion

The GFP is a small patch of cortex located in the posterior superior temporal sulcus (pSTS) that is activated by following the other's gaze towards a spatial target. We asked if activity in the GFP is essential for the observer's ability to follow gaze. In order to provide causal evidence, we disrupted information processing in the GFP in experiments in which monkey observers were alternatively asked to follow the other's gaze to a target or to shift their focus of attention to a distinct target based on a learned association between the other's identity and particular targets.

We found that electrical microstimulation of the GFP during the presentation of spatial information provided by gaze or identity cues caused a selective impairment of gaze-following (Fig. 2A) while sparing identity-mapping. By contrast, stimulation during the rule period had no effect on gaze-following, but perturbed identity-mapping (Fig. 3B). Prior electrophysiological exploration of the GFP (Ramezanpour and Thier, 2020) has identified neurons that exhibit spatial selectivity that link the spatial cue to the targets, as well as those that can discriminate between contexts before allowing this linkage to occur. We believe the properties of these neurons will help us explain the task-period-selective stimulus effect. It is likely that in the epoch in which gaze-following is taking place, perturbation of the GFP disrupted the activity of the spatially sensitive gaze-following (GF) neurons (see Fig. 5, inset), which make up the majority of task sensitive neurons discovered in the GFP (Ramezanpour and Thier, 2020). These gaze-following neurons have finely tuned preferences for different spatial targets and, importantly, neurons with different spatial preferences are intermingled. Considering the microstimulation parameters we may expect that microstimulation should have activated a larger of group neurons with varying spatial preferences, thereby compromising the transformation of information on the other's gaze into a precise spatial shift of attention. This is why gaze-following was impaired. The fact that gaze-following errors appeared random rather than reflecting a spatial bias is consistent with the notion of microstimulation activating a mixed bag of neurons with different spatial preferences.

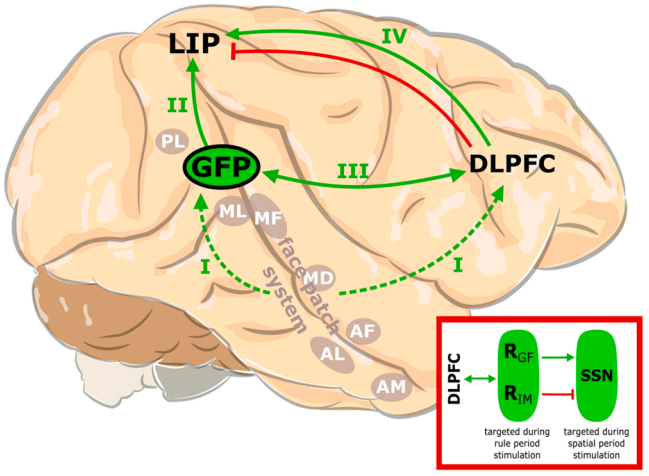

Fig. 5. Schematic of a potential cortical gaze-following network. A conceptual cortical network underpinning gaze-following and its executive control. Please see the discussion for further explanation. Face patches: anterior medial (AM), anterior lateral (AL), anterior fundus (AF), middle dorsal (MD), middle lateral (ML), middle fundus (MF), posterior lateral (PL). Gaze-following patch (GFP), lateral intraparietal area (LIP), dorsolateral prefrontal cortex (DLPFC). Inset (red box): Different pools of neurons interacting within the GFP. Gaze-following rule selective (R_{GF}) neurons are proposed to be facilitatory while identity-mapping rule selective (R_{IM}) neurons may be inhibitory. As a consequence the pools will have opposing push/pull effects on the spatially selective neurons (SSN), stopping them in case the identity-mapping rule applies while facilitating them in case of the gaze-following rule. In the event gaze-following is impertinent, there is also feedback from the GFP to the DLPFC.

Also the disruption of rule selectivity by microstimulation in the preceding rule period could be led back to an inability of microstimulation to distinguish between neurons with different functional roles at the site of stimulation. The majority of rule selective neurons lack activity in the later gaze-following period, suggesting largely different pools. Here – as a consequence of microstimulation – we see identity-mapping failing (Fig. 3B) rather than gaze-following being impaired. Moreover, errors cannot be attributed to the monkey falsely adopting the gaze following rule (Fig. 3C and D). The consequence is that the monkey exhibited an erroneous tendency to shift attention to the two targets in the set, identified neither by the identity-mapping nor by the gaze-following rule. Finally, because of the lack of temporal specificity, muscimol injections will indiscriminately shut down all neurons in the GFP, the ones representing the rule and the others that represent spatial locations indicated by gaze – the "effector" neurons. As the latter will be dysfunctional, the ability to follow gaze will be compromised, no matter which rule may prevail. However, as a possible alternative pathway remains intact (which we will go on to discuss), the clear bias to undergo identity-mapping when the gaze-following rule applies seems likely.

These observations clearly support a causal role of the GFP in controlling gaze-following. Our interpretation of these findings relies on two – as we see it – plausible assumptions, and allow us to propose a tentative prefronto-temporo-parietal network for gaze-following in which the GFP occupies a central position, allowing it to launch gaze-following if pertinent and to veto it if not (Fig. 5). Our two assumptions are as follows: 1) Gaze-following is a default behavior (Marciniak et al., 2015), which can unfold in the absence of cognitive control input. 2) Identity-mapping is a more elaborated behavior that requires both the suppression of gaze-following at the level of the GFP and lateral intraparietal area (LIP) as well as feedback on the successful suppression. Only then the gate for the flow of information on the target singled out by identity from the dorsolateral prefrontal cortex (DLPFC) to LIP will be opened up; the former which may function as a potential cognitive control center. Microstimulation of the GFP during presentation of the rule to map identities, disrupting the feedback from the GFP to DLPFC (Fig. 5, III), will compromise the realization of the identity-mapping rule. An erroneous fall back realization of the default gaze-following behavior will be prevented by undisturbed cognitive control exerted on LIP, vetoing the choice of targets that would be identified by gaze (Fig. 5, V). As a consequence, we see a break through behavior. As the monkey is trained to make a saccade to one of the 4 possible targets in order to be rewarded, they will tend to choose one of the two whose representations are not affected by the combination of condition and manipulation (Fig. 3C and D).

A preceding feature of the conceptual model is that it assumes that information on gaze direction reaches the GFP from members of the neighboring face patch system (Fig. 5, I). This is suggested by the fact that neurons in several members of the face patch system such as ML, MD and MF are known to be sensitive to the passive vision of head direction (Freiwald and Tsao, 2010; Yang and Freiwald, 2021; Perrett et al., 1985; Tsao, 2006; Fisher and Freiwald, 2015). Note that other parts of the monkey brain (Yang and Freiwald, 2021; Perrett et al., 1985; De Souza et al., 2005; Dal Monte et al., 2022; Pryluk et al., 2020) have been shown to be sensitive to eye gaze too. Also they can be expected to provide useful information on the other's focus of attention. They are not included in our schema as our experiments focused on head gaze stimuli rather than eye gaze cues, whose significance as drivers of monkey gaze-following is still contentious (Tomasello et al., 2007; Kobayashi and Kohshima, 2001; Shepherd, 2010; Perea-García et al., 2019). One should also take into account that none of the brain regions mentioned as potential sources of input to the GFP – no matter if specific to head or eye gaze and if mentioned in our schema or not – has been tested on gaze-following. While several of them have been examined in causal experiments, the focus has been on identity perception (Moeller et al., 2017) and attention to faces (Dal Monte et al., 2015) or the eye

region (Taubert et al., 2018) respectively. However, it remains unclear if the perceptual deficits observed entailed compromised gaze-following as the relevant behavioral paradigms were not deployed. Hence we currently lack causal evidence supporting the assumed link to gaze-following and the GFP.

Another major connection our model posits is one that allows the GFP to hand information on the location of objects singled out by the other's gaze over to the lateral intraparietal area (LIP), the latter thought to execute the shift of attention. An interaction between the GFP and LIP seems likely both on anatomical and physiological grounds. Tracer injections into the LIP have revealed projections originating from a region in the pSTS that may involve the GFP (Baizer et al., 1991). Neurons in the macaque area LIP have been shown to respond to shifts of attention to targets identified by the other's gaze (Shepherd et al., 2009), in line with its interpretation as a representation of a priority map (Fecteau and Munoz, 2006). In such a retinotopic representation of the visual field, different locations compete for attention. The most relevant one will win out over all the others and attract the attentional spotlight. The salience of a particular location can be cranked up by a variety of influences, including the other's gaze direction. Indeed a region in posterior parietal cortex in humans ("hLIP"), usually taken as the equivalent of monkey area LIP (Sereno et al., 2001), exhibits similar BOLD responses, no matter if shifts of attention are prompted by the other's gaze or alternative cues (Kraemer et al., 2020). Our demonstration of compromised gaze-following due to reversible lesions of the GFP suggests that the hypothesized impact of gaze on the LIP priority map is indeed originating from there.

The GFP may have two functions. Firstly it may serve as an interface needed to transform information on the other's head, eye direction and arguably also body orientation into a spatial pointer able to boost the priority of particular locations in the representation of space in LIP (Fig. 5, II). Secondly the results of the present study also clearly suggest a role for the executive control of gaze-following. Although the urge to follow the other's gaze is compelling, it can be suppressed if demanded by the given context, albeit not completely (Marciniak et al., 2015; Ricciardelli et al., 2013). The executive control of gaze-following was probed in our study by providing a rule asking the observer to exploit the other's gaze to allocate spatial attention or, alternatively, to suppress gaze-following and to shift attention guided by information on the other's identity. The fact that microstimulation of the GFP in the rule period compromised the application of the identity-mapping rule but not the gaze-following rule is consistent with the view that gaze-following is the default behavior mediated by the GFP that is suppressed if inexpedient.

The source of the control signal opening or closing the GFP gate is a matter of speculation at this point. However, a very promising candidate structure is certainly the dorsolateral prefrontal cortex (DLPFC) as numerous studies have established its general role in the cognitive control of behavior (Miller and Cohen, 2001; Rougier et al., 2005). Moreover, in a recent study on the volitional control of human gaze-following we could indeed identify BOLD activity in the DLPFC evoked by the need to suppress gaze-following (Breu, 2023). While previous attempts to trace the connections of monkey prefrontal cortex with other parts of cerebral cortex have shown projections to the STS (Yeterian et al., 2012), the limited resolution of the connectivity maps available does not allow one to decide if the GFP might indeed be a potential recipient of prefrontal afferents conveying information on the prevailing rule. However, no matter what its source may be, we know that information on the rule is available in the GFP as a substantial number of GFP neurons respond during the presentation of the rule. GFP neurons exhibit preference for either identity-mapping or gaze-following and typically show a consistent preference in the spatial cueing period that follows (Ramezanpour and Thier, 2020).

While the single unit data do not allow one to assign definite circuit positions to these two groups of GFP neurons, our virtual lesion data may suggest that those preferring identity-mapping could be inhibitory neurons controlling excitatory neurons activated by gaze cues, thus promoting gaze-following (Fig. 5, inset). Depriving the latter of their drive should compromise gaze-following, while disrupting the information to suppress gaze-following would lead to more false gaze-following decisions, both in accordance with our results. Finally, the fact that identity-mapping is spared during manipulations of the GFP in the spatial cue period could be easily explained by a pathway linking information on identity with distinct spatial positions that bypasses the GFP (Fig. 5, I & IV). The conceptual model assumes that this pathway has the same origin in the DLPFC as the one for the cognitive control of gaze-following. In more general terms, we posit a specific pathway for gaze-following through the GFP, supplemented by a parallel, generic prefronto-parallel pathway for shifts of attention able to tap any source of information for the guidance of attention, and moreover, giving priority to this source by controlling the GFP. A similar schema would easily account for the finding of normal arrow-following versus impaired gaze-following in the temporal lesion patients studied by Akiyama et al (Akiyama et al., 2006b).

How sure can we be that the GFP is indeed a controller of attention that is limited to exploiting the other's gaze? There are several observations that might in fact suggest a broader role. Their common basis is the observation that the guidance of attention by non-gaze cues may involve information processing in parts of the STS that might possibly overlap with the GFP (Ramezanpour and Fallah, 2022). For instance, compromised spatial attention guided by motion (random dot motion) and non-motion cues (in the form of second order orientation stimuli) following reversible inactivation of the superior colliculus or the frontal eye field are correlated with a drop in BOLD activity in a region on the middle STS (anterior floor of the superior temporal area and area IPa in the sulcal floor). Moreover, a similar attentional deficit could be evoked by direct inactivation of the very same area in the STS (Bogadhi et al., 2019). Also a more posterior area, pITd (posterior inferotemporal cortex area) has been implicated in attentional selection based on a few visual features including visual motion and color (Stemmann and Freiwald, 2019). While the pITd and the GFP are probably not too far apart from each other, the presumed independence of the former from the specifics of the attention guiding cues speaks against the possibility that pITd might be congruent with the GFP. After all GFP neurons were usually interested in the specifics of the attention-guiding cues, being in most cases selective for gaze and in rarer cases for identity information but unresponsive to shifts of attention guided by abstract objects (Ramezanpour and Thier, 2020). Moreover, as mentioned before, the causal interference findings strongly argue for clearly different roles of information on the other's gaze and identity. The anatomical distinction between the GFP and pITd can be further supported by the fact that the same areas in the human brain are much further apart (Marquardt et al., 2017; Sani et al., 2021).

The anatomical location of the GFP is also close to cortical areas involved in visual motion processing including FST (fundus of the superior temporal area), LST (lower superior temporal), MT (middle temporal) and MST (medial superior temporal) located close to the posterior end of the STS (Nelissen et al., 2006). Integrating visual motion and form is necessary for the perception of the dynamic aspects of faces (Fisher and Freiwald, 2015). It has recently been shown that MD neurons are tuned to eye motion and other aspects of facial movements (Yang and Freiwald, 2021), although the behavioral role of these preferences remains unknown. The GFP seems to be much closer to FST than to the other motion areas MST, MT, LST or the more rostrally located MD face patch. Considering that even a change of a straight-ahead looking portrait to one looking at one of the spatial targets as in our paradigm will induce a percept of motion underpinning gaze-following, the observed proximity of the GFP and a motion processing area like FST is hardly surprising. In other words, GFP neurons may draw upon information provided by motion processing units in neighboring areas such as the FST in order to shape their spatial tuning. It is currently unknown whether or not static views of gazing faces can evoke gaze-following

responses in the GFP as to the best of our knowledge all studies have involved a form of transition from a forward facing frame to gaze directed towards particular locations or objects.

To sum up, this study has provided causal evidence for a central role of the gaze-following patch (GFP), a distinct region located on the lower bank and the fundus of the posterior STS, in allowing monkeys to use the other's gaze to shift their own attention to targets that the other is interested in. Together with complementary information from previous studies, our findings suggest a key role of the GFP in driving gaze dependent shifts of attention and in vetoing them if not pertinent.

4. Materials and methods

4.1. Animals and surgery

The two male rhesus macaques (*Macaca mulatta*) that had participated in a previous electrophysiological study to characterize their respective GFPs (Ramezanpour and Thier, 2020) were used in the present study (T and L; weights 8 and 11 kg respectively). Each monkey had received structural MRI scans to ascertain the precise location for a titanium chamber for accessing the STS, and a titanium head-post for restraining the monkey's head during experimentation. Additionally, scleral search coils were implanted for eye position recordings. All surgical interventions were carried out under combination anesthesia consisting of isoflurane (1.3%) and remifentanil (1–2 μg per kg per minute), and the careful monitoring and control of body temperature, heart rate, blood oxygen saturation, and blood pressure. Opioid analgesics (buprenorphine) were administered until the monkeys did not show any signs of residual pain, and experiments commenced not sooner than 12 days after surgery at the earliest, at a time the animals had fully recovered. Once the animals had become proficient with the behavioral tasks (after 6–12 months) the skull was trepanated inside the implanted chamber for the start of electrode penetrations, resorting to the aforementioned surgical/postsurgical protocols. All experimental preparations and protocols were approved by the local animal care committee (Regierungspräsidium Tübingen, Abteilung Tierschutz) and fully complied with German law and the National Institutes of Health's Guide for the Care and Use of Laboratory Animals.

Because monkey L had also been involved in a prior fMRI study that had led to the discovery of the GFP based on gaze-following related BOLD activity (Marciniak et al., 2014), we could take advantage of the stereotactic data afforded by that study to determine where best to place the recording chamber for targeting the GFP. In monkey T, we took the average location of the GFP in the two monkeys used in the fMRI study to estimate the most promising location for placing the recording chamber.

4.2. Behavioral paradigms

The two monkeys were trained in a gaze-following paradigm which necessitated the use of either gaze, or identity information provided by the head of a demonstrator monkey. We refer to these two tasks that call upon these two behaviors as the gaze-following and identity-mapping tasks respectively. The trials of these two tasks were interleaved with each other in a pseudo-random manner, and the timing and presentation of all events were essentially identical, differing only in one aspect, the instruction to undergo gaze-following or identity-mapping which we will go on to describe below.

The individual trials began with a white fixation point on a black background, which was to be fixated upon for 500 ms. Afterwards, a neutral forward-facing monkey head was presented behind the white fixation cue. The white fixation cue would change its color 400 ms later to either red or green, informing the subject monkey if gaze-following or identity-mapping would be required. The period in which the rule cue was presented ("rule period") lasted for another 400 ms before the appearance of another demonstrator monkey's head with its head direction averted, in place of the previously neutral forward-facing monkey head. Simultaneously, four spatial targets appeared before the demonstrator monkey's head; both stayed until the end of the trial and this formed the spatial cue/target period aforementioned in the main text. The disappearance of the red/green rule cue 350 ms afterwards served as a go signal to the subject monkey to make a saccade towards one of the four targets.

In the gaze-following condition, indicated by the red rule cue, the monkey was required to use the head-gaze information provided by the demonstrator and make a saccade to the target singled out by the latter's gaze direction. However, if identity-mapping was called for by presenting a green rule cue, the monkey had to ignore the head gaze signal, and instead rely on learned associations of the demonstrator's identity with the spatial targets. There were four identities to be learned, one corresponding to each spatial target available, and each time the monkey came across a certain identity, irrespective of the demonstrator's head direction, it would report its identity by making a saccade to the respective target. The monkeys were rewarded with a drop of juice or water if they successfully maintained fixation on the central fixation point and later made a saccade towards the target appropriate to the rule. If the monkeys were unable to maintain their fixation within the 2° by 2° window around the central fixation point, or failed to choose the correct spatial target within 300 ms after the go signal, the trial was aborted and left unrewarded.

Images of monkeys with averted and neutral forward-facing head directions were 5.6° by 5.6° in size, and were centered on the fixation cue described above. The four spatial targets were composed of red dots (each 0.8° in diameter) arranged in a virtual horizontal line 1° below the center of the monkey portraits. The horizontal eccentricities of the targets with respect to the monkey subject were −10°, −5°, 5°, and 10° (or −40°, −20°, 20°, and 40° with respect to the gazing demonstrator monkeys). As there were four monkey identities involved in the paradigm, with each identity gazing in four possible directions, a total of 16 stimuli were used which are summarized in Fig. 1B.

4.3. Electrical microstimulation

Per microstimulation session, a single glass-insulated tungsten microelectrode (1 MΩ at 1 kHz; Alpha Omega Engineering, Nazareth) was lowered into the recording chamber via a homemade multichannel micromanipulator. The stimulation sites for the GFP and control area were in accordance with the meticulous topographical maps afforded by the single unit recordings performed in monkeys T and L in the study of Ramezanpour (Ramezanpour and Thier, 2020). The core of the GFP was designated as the position where the contrast between gaze-following neurons with identity-mapping neurons was highest, also referred to as the 'hotspot' on the ventral bank of the pSTS, and we performed stimulations within a 1 mm radius around said core. Under the assumption that the pyramidal cell excitability constant of the pSTS is comparable to that of V1 (Klink et al., 2021; Ranck, 1975; Tehovnik et al., 2006), neurons inside a sphere of about 0.5 mm radius may be expected to be influenced by our current size. The organization of the GFP is comparable to that of face patches (Aparicio et al., 2016), in that the boundaries of the GFP are not sharp, and some gaze-following neurons can still be found many millimeters away from the core of the GFP. However, our microstimulation spread falls within the GFP hotspot, which is around 1 mm in size (Ramezanpour and Thier, 2020), and sufficiently far away from the center of the chosen control area (4 mm anterior to the GFP).

Once the electrode was inserted into the area of interest and robust multiunit activity could be detected, microstimulation sequences could be delivered while the monkey performed the paradigm using the Stimulus Generator 4002, Multichannel Systems. Each stimulation train was 350 ms long, and consisted of biphasic current pulses 0.2 ms in duration and 0.1 ms in between the cathodal (leading) and anodal phases. In different experiments the train of electrical current (200 μA at

200 Hz) started either at 900 ms, i.e. at the onset of the rule period, or later at 1300 ms relative to trial onset at the time, when spatial information provided by gaze and identity respectively was provided. In either case, stimulation lasted for 350 ms. Trials with and without stimulation had a probability of 50% and were randomly interleaved. Combined with the testing of both gaze-following and identity-mapping within the same session, it was unlikely any adaption or compensation strategies were induced with respect to stimulation or the different rule conditions. For the recording of all eye movement data, randomization and timing of the stimulation trains as well as the presentation of the visual material, we deployed an in-house data acquisition and stimulation software package (nrec, http://nrec.neurologie.uni-tuebingen.de/nrec).

4.4. Muscimol injections

Following our microstimulation experiments that allowed us to further narrow down GFP coordinates that consistently delivered gaze-following impairments upon microstimulation, we targeted muscimol injections into the same site. The control area was also the same as the one chosen for microstimulation. Micropipettes were prepared from custom glass capillaries (outer diameter 0.5 mm, inner diameter 0.33 mm, Hilgenberg) and a P-30 Micropipette puller (Sutter Instrument, Novato). The micropipettes were filled with muscimol (10 μg/μl, M1523 Sigma), and glued to a modified 10 μl Hamilton syringe that was prefilled with a paraffin oil/Sudan Black mix, before being inserted into a 20 G metal cannula and retracted a few mm before penetrating the dura. The micropipette/syringe assembly was then driven into the cortex at a speed of 12 μm/s via a micropositioner (David Kopf Instruments Model 650) until it reached the area to be inactivated. We waited 5–15 mins after the glass capillary had reached the goal position before commencing injections. Typically 2–2.8 μl of muscimol, or saline in the case of control injections were injected, at a rate of 0.1 μl/min. The movement of the paraffin/dye, air bubble and drug interface allowed us to gauge the volume injected. The glass micropipette was then slowly withdrawn from the brain at 12 μm/s before behavioral testing commenced. Approximately 15 mins elapsed from the completion of the injection before behavioral testing began, and completion of the task trials necessitated 1–1.5 h, well within the expected time period in which muscimol was expected to remain effective.

4.5. Statistical analysis

For each microstimulation session in a given cortical area (GFP or control area), we divided the paradigm into its constituent gaze-following and identity-mapping trials, and further separated them into pools of stimulated or unstimulated trials. We determined the mean performance for each pool (percentage of trials correct), grouped the performance for each task (gaze-following or identity-mapping) for each cortical area (GFP or control), and performed a non-parametric pairwise t-test (Wilcoxon t-test) between the stimulated and unstimulated conditions. This allowed us to find out if microstimulation produced any change in behavior for a given task, in a given cortical area.

In order to gauge the impact of microstimulation on gaze-following unaffected by possible differences in performance between experimental sessions unrelated to microstimulation we calculated a normalized gaze-following index (GFI) per session according to:

$$GFI = \frac{G_{Stimulated\ Performance} - G_{Unstimulated\ Performance}}{G_{Stimulated\ Performance} + G_{Unstimulated\ Performance}}$$

Correspondingly, an identity-mapping index (IMI) was calculated for each session to investigate the normalized performance change for identity-mapping according to:

$$IMI = \frac{I_{Stimulated\ Performance} - I_{Unstimulated\ Performance}}{I_{Stimulated\ Performance} + I_{Unstimulated\ Performance}}$$

Two possible types of errors could be evoked by the microstimulations: a bias for identity-mapping when undergoing gaze-following and vice versa, or a bias towards a specific spatial target. To investigate the former type of error in the context of impairments during gaze-following, we first checked if the spatial target selected in all unstimulated gaze-following error trials happened to correspond to the behavior demanded by the application of the identity-mapping rule (as if the trials had required identity-mapping in the first place); this helped to establish the monkey's baseline tendency to make identity-mapping mistakes during gaze-following. This was repeated with the stimulated conditions. We then compared the performance in the stimulated and unstimulated conditions across all sessions using Wilcoxon signed-rank tests. The same procedure was applied to identity-mapping trials. Effect sizes are reported via Cohen's d values.

To identify a possible post-stimulation spatial target bias in the GFP, we grouped gaze-following trials according to the four spatial targets, and for each target calculated the errors made to each of the other targets. For these uncued targets we performed a Kruskal-Wallis ANOVA test comparing target preferences before and after microstimulation for changes in the idiosyncratic target bias patterns. Pairwise t-tests were performed for each uncued target before and after microstimulation.

Analysis of the muscimol behavior data proceeded in a similar manner as the microstimulation analysis, with the primary difference being that statistical tests were unpaired as each session was either designated "inactivated" (with muscimol) or "control" (without injection or with saline).

Funding

This work is supported by the Deutsche Forschungsgemeinschaft (DFG) [TH 425/12–2, TH 425/17–1, to P.T.] and the Werner Reichardt Centre of Neuroscience [EXC 307, to P.T.].

CRediT authorship contribution statement

I.C., H.R., and P.T. designed research; I.C. performed research; I.C. analyzed data; I.C., H.R., and P.T. wrote the paper; P.T. developed the conceptual framework; I.C., H.R., and P.T. contributed to discussing analysis.

Declaration of Competing Interest

The authors declare no competing interests.

Data Availability

Data will be made available on request. Data for this research article have been deposited at Figshare (10.6084/m9.figshare.21183841).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pneurobio.2023.102466.

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