

1 **Title**

2 • **Visual Cortical Area MT is Required for Development of the Dorsal**

3 **Stream and Associated Visuomotor Behaviours**

4 • The Early Life Contribution of MT to Visuomotor Behaviour

5

6 **Authors**

7 William C. Kwan¹†, Chia-Kang Chang¹†, Hsin-Hao Yu², Inaki C. Mundinano¹, Dylan M.

8 Fox¹, Jihane Homman-Ludiye¹, James A. Bourne¹*

9

10 **Affiliations**

11 ¹ Australian Regenerative Medicine Institute, Monash University, Clayton, VIC 3800, Australia.

12 ² Department of Physiology, Monash University, Clayton, VIC 3800, Australia.

13 † Authors contributed equally

14 *Corresponding Author email: James.Bourne@monash.edu

15

16

17

18

19

20

21

22 **Abstract**

23

24 The middle temporal (MT) area of the extrastriate visual cortex has long been studied in
25 adulthood for its distinctive physiological properties and function as a part of the dorsal stream,
26 yet interestingly possesses a similar maturation profile as the primary visual cortex (V1). Here we
27 examined whether an early-life lesion of MT altered the dorsal stream development and the
28 behavioural precision of reaching to grasp sequences. We observed permanent changes in the
29 anatomy of cortices associated with both reaching (PE and MIP) and grasping (AIP), as well as in
30 reaching and grasping behaviours. In addition, we observed a significant impact on the anatomy
31 of V1 and the direction sensitivity of V1 neurons in the lesion projection zone. These findings
32 indicate that area MT is a crucial node for the development of the primate vision, impacting both
33 V1 and areas in the dorsal visual pathway known to mediate visually guided manual behaviours.

34

35 **Teaser**

36 The early life loss of visual area MT leads to significant anatomical, physiological and
37 behavioural changes.

38

39 **MAIN TEXT**

40

41 **Introduction**

42 Vision relies on a multiplicity of areas within the brain to communicate synergistically in order
43 to produce an accurate percept. The seminal works of Goodale & Milner(1) and Ungerleider &
44 Mishkin(2) proposed the existence of two neocortical pathways which have a dichotomous visual
45 functional specialisation. More specifically, the dorsal stream pathway is involved in perceiving
46 motion and “vision-for-action”, while the ventral stream pathway is associated with shape/ object
47 perception and “vision-for-perception”. Central to the dorsal stream is the middle temporal (MT)
48 area (**Fig. 1A, B**). Based on established anatomical markers of neural circuit maturation, area MT
49 matures early and in parallel with primary sensory areas, including the primary visual cortex
50 (V1)(3). Further, since the monosynaptic V1-MT connection is yet to be fully established during
51 this process, the early maturation of MT is thought to be independent of V1 input(4). This
52 knowledge, and the fact that MT has a first-order topographical map(5) and is directly recipient
53 of thalamic connections(6, 7), supports the notion that it is a ‘primary-like’ area and serves as an
54 anchor early in life to support establishment of the dorsal stream(8).

55

56 In adulthood, MT receives significant input directly and indirectly from V1(5, 9), and is
57 interconnected with multiple dorsal stream extrastriate areas, including V3 and the dorsomedial
58 (DM) area, anterior and lateral intraparietal areas (AIP and LIP) (10–13) and the frontal eye
59 fields (FEF)(14, 15) (**Fig. 1A, B**). Area MT also has abundant connections with subcortical
60 structures, including reciprocal connections with the medial portion of the inferior pulvinar(4, 7,
61 16), and afferent projections from the koniocellular layers of the lateral geniculate nucleus
62 (LGN) (6) and superior colliculus (11, 17, 18).

63

54 A substantial proportion of neurons within MT are highly tuned for direction(19, 20), a clear
55 distinction from V1, suggesting that MT plays a central role in motion perception and integration
56 of visual information. However, there are few studies which have interrogated how injury to MT
57 impairs visual perception and global visual behaviour. Newsome and colleagues(21, 22)
58 provided behavioural evidence of how MT contributes to motion perception following
59 mechanical ablation of MT, while motion blindness/ akinetopsia has been observed clinically in a
70 patient with bilateral MT injury(23, 24). Further, others have demonstrated that V2 direction
71 tuning properties are dependent on MT(25).

72

73 In the phenomenon of blindsight, the extensive multiplexed circuitry of the dorsal stream, with a
74 central component being area MT, has been long implicated as the neural substrate that affords
75 the ability to perform specific visually-driven tasks in the absence of V1(26, 27). More specific
76 investigation revealed that MT remains active when visual stimuli are presented within the
77 scotoma(28, 29).

78

79 Few studies have considered the role of MT in the development of the dorsal stream and to the
80 establishment of specific visuomotor behaviour but developmental studies have inferred that MT
81 acts as the primary node the establishment of the dorsal stream(3, 30). Further, early-life lesions
82 of the geniculostriate pathway have highlighted the conserved integrity of MT in both humans
83 and monkeys (27, 31). Therefore, we hypothesised that an early-life lesion of MT will
84 permanently perturb reaching to grasp behaviours and result in dysfunction of areas directly
85 connected with MT.

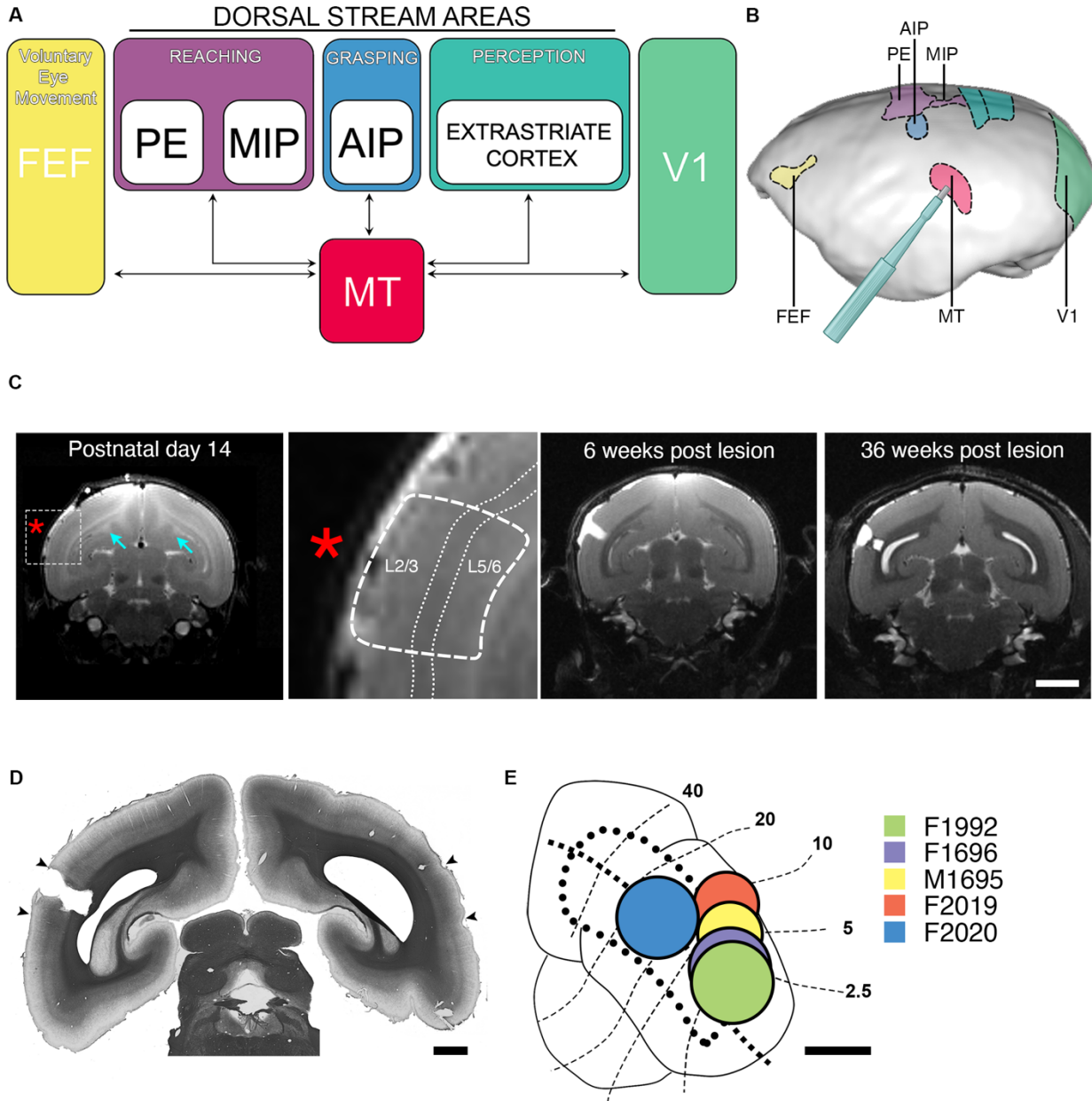
86

87

88

39 **Results**

39 We used early postnatal ablations as a method to study the role MT would serve in the
40 development of the visual cortex and visually-guided behaviours. At 6 weeks post-surgery, MRI
41 T2-weighted images were acquired to validate unilateral biopsy punch ablation of MT in the 5
42 neonatal (PD14) marmosets (**Fig. 1C**). Prior to lesion, the location of area MT was visualised in
43 MRI images (T2-weighted) by a dorsal shift in layer 4 from adjacent areas (**Fig. 1C inset**).
44 During the excision of MT tissue, particular care was taken to remove all 6 cortical layers while
45 leaving the underlying white matter tract intact. When the animals subsequently reached young
46 adulthood (>36 weeks) and underwent DTI scans for evaluation of effected cortices, another T2
47 sequence was obtained to map the extent of the lesion (**Fig. 1B**). In these scans, we often
48 observed that the lesion core had scar tissue and subtle degeneration of the underlying white
49 matter had occurred. Following perfusion of the cerebral tissues, histological confirmation of the
50 lesion was achieved with a Gallyas (myelin) silver stain (**Fig. 1D**), and the lesion was fully
51 reconstructed to establish its topographical extent for each animal (**Fig. 1E**).
52
53



05 **Figure 1. Direct connectivity of middle temporal (MT) area of the visual cortex and**
06 **unilateral early life lesion approach.**

07 **(A)** Wiring diagram detailing monosynaptic reciprocal connectivity of area MT and proposed
08 behavioural function. **(B)** Lateral view of left hemisphere of marmoset cortical surface
09 highlighting anatomical positioning of areas in **(A)**. **(C)** T2-weighted MRI of a marmoset brain at
10 the level of parafoveal MT, which was targeted for ablation at PD14. MT was demarcated based
11 on dorsal shift in the layer IV (left image, red asterisk and inset). In the anterior/posterior plane,
12 the core of MT was denoted as when the most caudal aspect of the corpus callosum becomes
13 visible (arrow). Further T2-weighted scans were conducted at 6 weeks and 1 year post-injury to
14 confirm lesion location and also diffusion tractography imaging (DTI) for fractional anisotropy
15 analysis (DTI results in **Fig. 4**, scale bar = 5mm). **(D)** Histological analysis with myelin silver
16 staining for *ex vivo* demarcation of lesion (scale bar = 2mm) **(E)** Summary of the extent, and
17 retinotopic relationship, of MT lesion in each lesioned animal (scale bar = 2mm). Details of the
18 experimentation each animal underwent is further detailed in **Table 1**.

19

20 **The absence of MT during development perturbs reach and grasp kinematics as well as**
21 **interaction with static and moving objects**

22 As MT neurons are highly tuned for direction and the perception of motion, we wanted to
23 determine if accurate reward-driven visuomotor behaviour was still achievable following early-
24 life loss of MT. To ensure adequate compliance with the task, we first trained the animals to enter
25 a removable transport box on the home cage, which was then taken into the behaviour laboratory
26 (**Fig. 2A**)(32). We employed naturalistic, goal orientated, reach and grasp tasks once neonatal MT
27 lesion animals (PD14) had reached adulthood (>18 months). These were undertaken both
28 statically (**Fig. 2B**) or upon a variable speed/ direction turntable (**Fig. 2b**). Each food retrieval
29 trial was 2D video-captured (see camera; **Fig. 2A**), which allowed us to study the animal's
30 proficiency in executing the task and the kinematics of the reach and grasp phases.

31
32 Animals were first presented with a static task. The task involved presenting a food reward which
33 was placed on a pedestal in front of the animal (**Fig 2B - D**). Food rewards were cut into two sizes
34 of cuboid (*small*: ~5x5 mm face; and, *large*: ~10x10 mm face) and were first employed to
35 determine if the object size would affect overall performance. No significant difference in
36 retrieval performance was observed between the two sizes of fruit reward in both control and
37 lesioned cohorts (ANCOVA $F(1,52)=0.68, p=0.41$)(Fig S1A, B). When examining the collective
38 retrieval attempts of both sizes of the statically presented food reward, we found overall
39 performance within the MT-lesioned group was significantly impaired when compared with
40 controls (permutation test, $p=0.04^*$)(**Fig. 2E**). Further analysis of the reach and grasp kinematics
41 revealed significant differences in hand preshaping and reaching behaviour. Specifically, during
42 the preshaping phase, neonatal MT-lesioned animals exhibited a significantly larger maximum
43 grip aperture than controls (permutation test, $p=0.0037$) (**Fig. 2F**). Further characterisation of the
44 behaviour revealed neonatal MT-lesioned animals exhibit a feedforward movement with greater

45 velocity (permutation test, $p=0.04$) (**Fig. 2G**) and acceleration (permutation test, $p=0.02$)(**Fig. 2H**)
46 when approaching the target object.

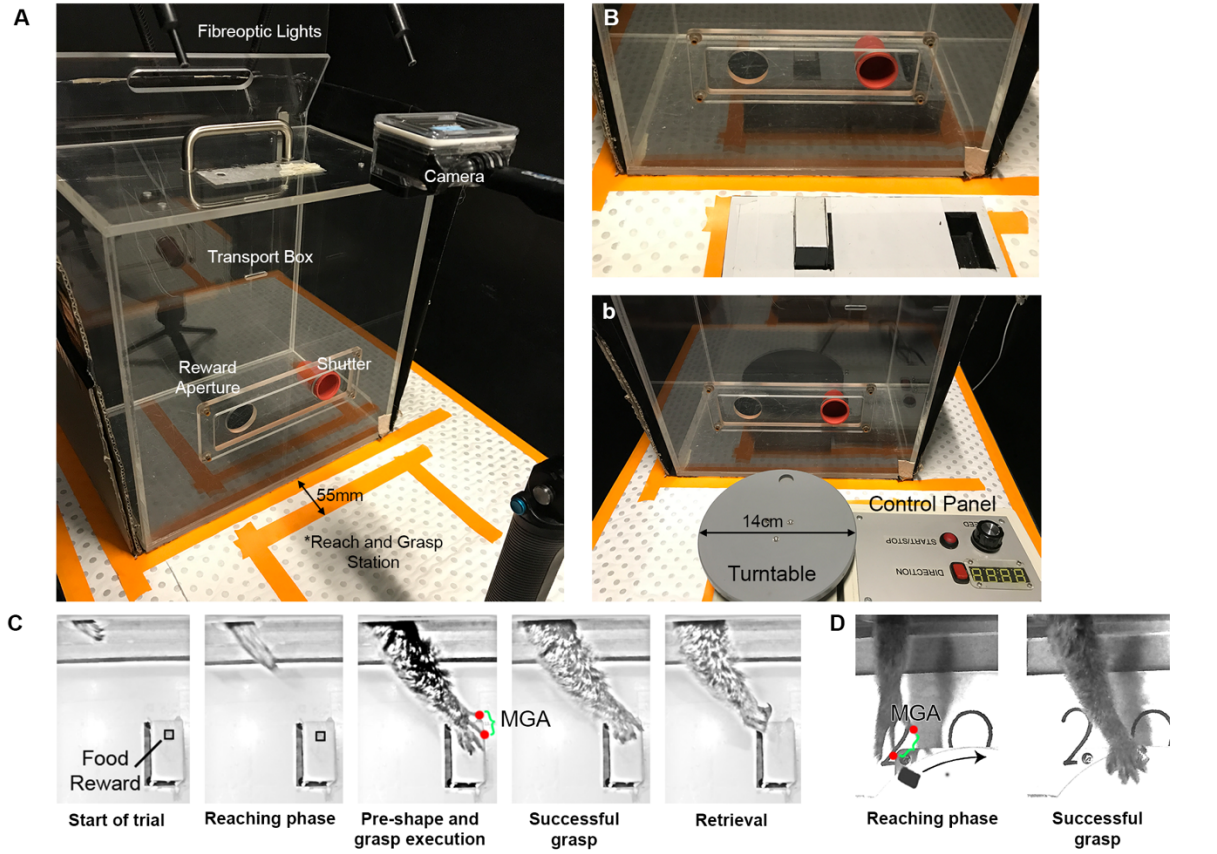
47

48 We further assessed whether a target object of different sizes may influence the animal's ability to
49 pre-shape their hand. By plotting the object size against the MGA, a significant correlation was
50 observed between the two cuboid food pieces in the control group (Pearson's correlation,
51 $r(381)=0.16$, $p<0.01^{**}$)(Fig S1C). However, hand preshaping is not seen within the neonatal MT-
52 lesioned group (Pearson's correlation, $r(338)=0.05$, $p=0.33$)(Fig S1D).

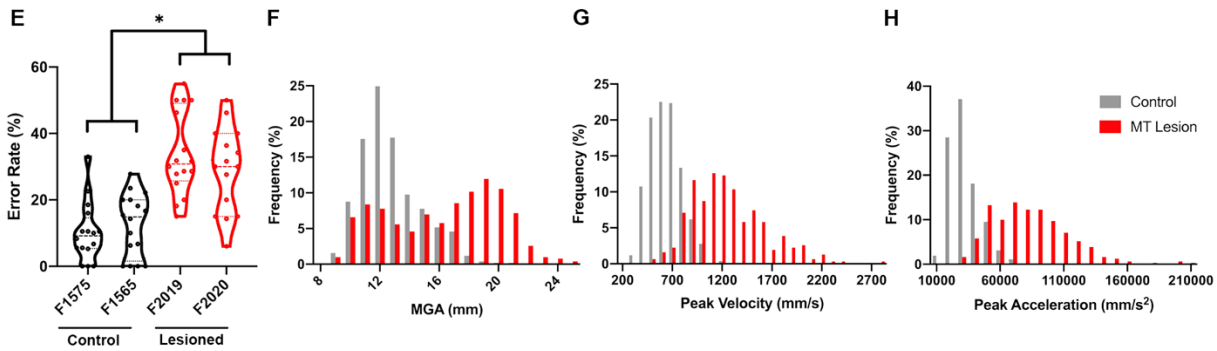
53

54 To interrogate the animal's ability to accurately engage a moving object in a naturalistic setting,
55 animals were again required to reach and grasp a food reward, but in this instance the reward was
56 placed on a variable speed/ direction turntable in front of the transport box (**Fig. 2b, I**). A
57 difference in object retrieval error rate was observed between the two cohorts, with the neonatal
58 MT-lesioned group having an increased error rate (permutation test, $p=0.042$) (**Fig. 2J**). Further
59 analysis of reach and grasp behaviour within the lesion cohort revealed that when retrieval of the
60 food reward was unsuccessful, this was largely due to executing their reaching action prematurely
61 (**Fig. 2K**). When lesioned animals failed in retrieval of moving objects, the magnitude of their
62 failure was greater compared to controls (permutation test, $p=0.003$)(**Fig. 2L**). Further, they were
63 less co-ordinated and consequently had less success in retrieval of the reward on their first attempt
64 (permutation test, $p=0.023$)(Fig. S1E). The MGA, peak velocity and acceleration observed
65 between both cohorts for the moving task were similar (Fig. S1F, G, H).

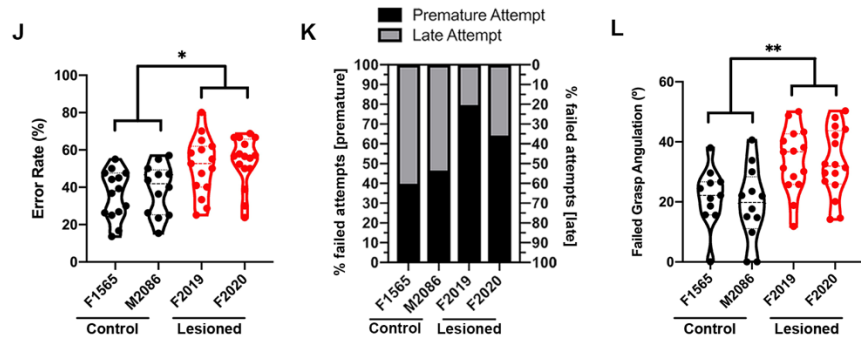
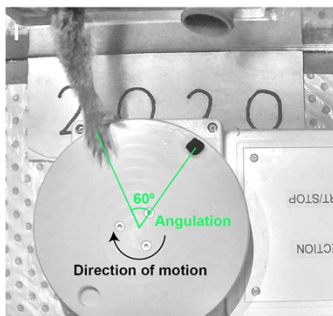
66



STATIC OBJECT TASK



MOVING OBJECT TASK



58 **Figure 2. Early-life MT lesions perturb goal orientated reach and grasp performance in**
59 **static and moving objects.**

70 **(A)** Experimental setup of reach and grasp tasks. The animal is presented with either a static task
71 **(B)** or moving task **(b)** (see methods for full details). **(C)** Example of 720p footage of an animal
72 successfully grasping a static reward. **(D)** Example of 720p footage of an animal successfully
73 grasping a moving reward. **(E)** Performance (error rate) of control vs lesioned animals in reaching
74 and grasping static objects. Lesioned animals performed significantly worse (permutation test,
75 $p=0.04^*$). **(F)** Frequency distribution across trials of maximum grip aperture (MGA) for control
76 and lesioned animals. Lesioned animals exhibit a larger MGA in their grasp and reach with
77 greater velocity **(G)** and acceleration **(H)**. **(I)** An example trial where the animal was delayed in
78 reaching for the food reward and failed in the moving object reach and grasp trial, the magnitude
79 of which was calculated. **(J)** Performance of control vs lesioned animals in reaching and grasping
80 moving objects. Lesioned animals performed significantly worse (permutation test, $p=0.042$). **(K)**
81 Failed trials within the lesioned cohort were largely due to the animal reaching prematurely.
82 Control animals showed close to a 1:1 proportion of premature and late reaching actions in failed
83 trials whilst MT lesioned animals exhibited a tendency to reach prematurely. **(L)** The average
84 magnitude of error as denoted by angulation in the failed trials. When lesioned animals failed in
85 reaching and grasping moving objects, the magnitude of the miss was greater than controls
86 (permutation test, $p=0.003$).

87

38 **V1 responses are altered following an early-life lesion of MT**

39 As there is a significant monosynaptic projection between V1 and MT, we wanted to observe if an
40 early-life lesion of MT impacted upon the response properties of neurons in the lesion projection
41 zone (LPZ) of ipsilesional V1 in adulthood. Visually evoked single-unit activity was recorded in
42 the LPZ of V1 from two animals (M1695 & F1696, **Fig. 3A**), with a total of 122 units recorded
43 from. Visual stimuli were presented to determine the orientation and direction selectivity as well
44 as optimal spatial and temporal frequencies for each of the units.

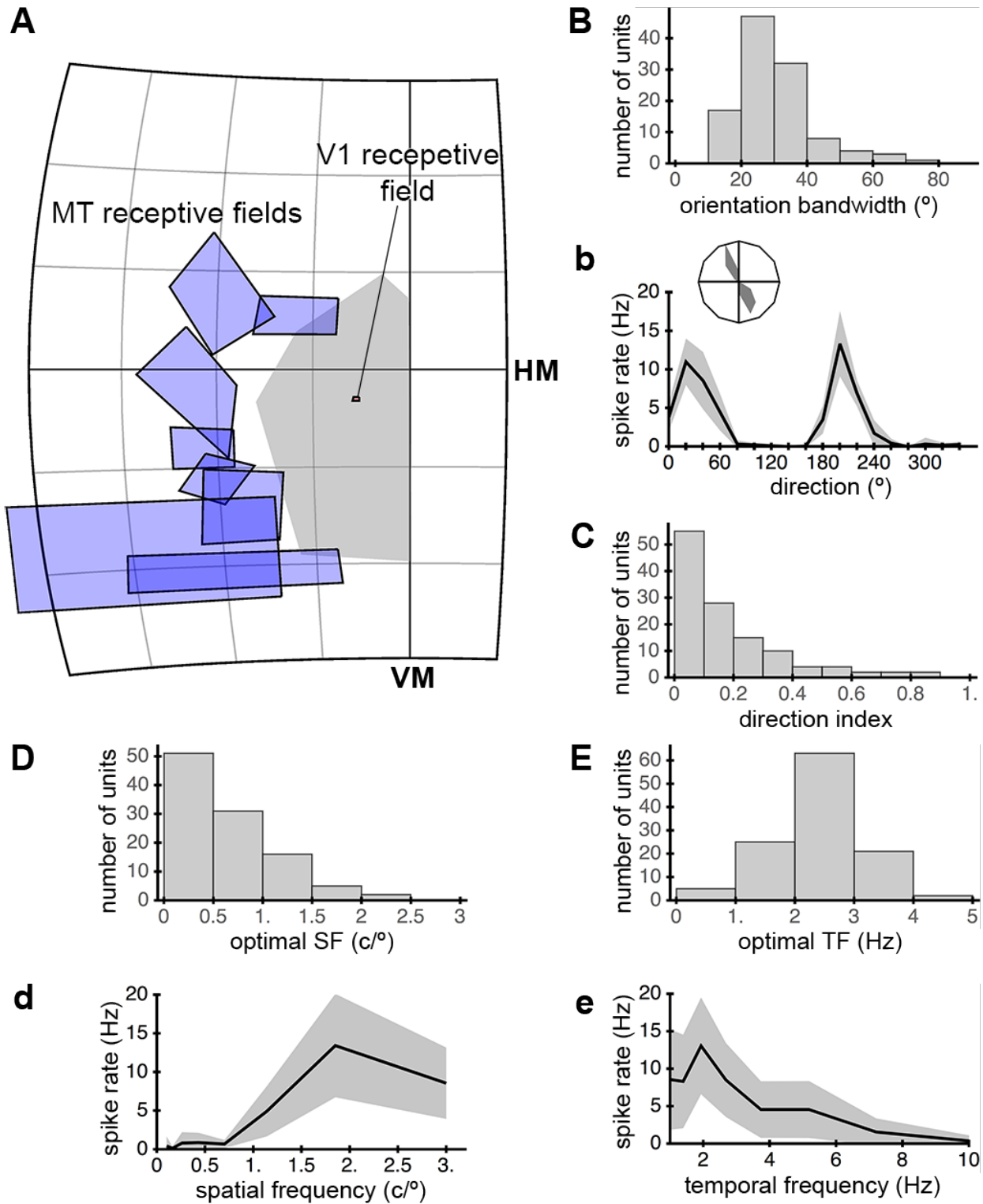
45
46 Our first observation was that the basic retinotopic organisation of V1 was unaffected by the
47 neonatal V1 lesion (**Fig. 3A**), which was expected. Our single-unit recordings revealed that 86.1%
48 (105 out of 122) of V1 neurons within the LPZ were found to be orientation selective. The half-
49 width-half-height (HWHH) bandwidth which is a traditional measure for orientation
50 selectivity(33, 34) within the MT lesion affected V1 was observed to be 29.5° (**Fig. 3B**). This is
51 comparable to the median HWHH bandwidth of 29.0° which has been reported previously for
52 normal V1 neurons throughout the entire visual field(35). Direction selectivity (DS) of a cell was
53 determined by calculating a direction selectivity index(35, 36), whereby an index of >0.5 suggests
54 the cell is tuned for direction. Previous reports within marmoset V1 demonstrate approximately
55 20% of V1 neurons are DS. Our findings were lower than this, with less than 10% (10 out of 122)
56 classified to be direction selective (DS) (**Fig. 3C**). Although the proportion of DS can vary with
57 eccentricity: central vision, 18% DS; near periphery, 26% DS; and, far periphery, 20% DS(35),
58 our observations of ~10% fell below this previously reported proportion.

59
60 Neurons in V1 within the two subjects responded optimally to a spatial frequency of 0.7 cycles/°
61 (**Fig. 3D**) and a temporal frequency 2.3 Hz (**Fig. 3E**). Previously determined values for optimal
62 spatial frequency was 1.08 cycles/° centrally and 0.45 cycles/° in the near periphery, with optimal

13 temporal frequency between 3.0-4.0 Hz across the entire visual field. Therefore, the
14 spatiotemporal sensitivities appeared unaffected by an early-life MT ablation.

15

16 Together, the basic retinotopic layout and physiological properties of V1 neurons appeared
17 unaffected by the early life MT lesion, with one exception. Namely, across the recorded areas,
18 the proportion of directionally selective neurons was lower than previously reported, suggesting
19 that MT may play a role in shaping these responses.



22 **Figure 3. Tuning properties of V1 neurons following unilateral MT lesion.**

23 **(A)** MT receptive fields were mapped by recording on the periphery of the lesion core. Following
24 receptive field mapping, the scotoma is delineated and single unit recordings of V1 neurons were
25 performed within the MT-V1 lesion projection zone (LPZ) (see methods for full details). **(B)** The
26 orientation selectivity of all recorded V1 neurons as determined by the half-width-half-height
27 bandwidth (Median HWHH = 29.5° from 122 units). **(b)** An example of the orientation tuning
28 curve of a V1 neuron within the LPZ. **(C)** Direction index of the 122 V1 units recorded within the
29 LPZ. A direction index of >0.5 suggests the neuron is directionally selectivity. Only 10 out of 122
30 (~8%) of neurons were tuned for direction. V1 neurons within the LPZ responded optimally to a
31 spatial frequency of 0.7 cycles/° **(D)** and temporal frequency of 2.3 Hz **(E)**. Examples of the
32 spatial **(d)** and temporal frequency **(e)** tuning curves from V1 neuron within the LPZ are shown.

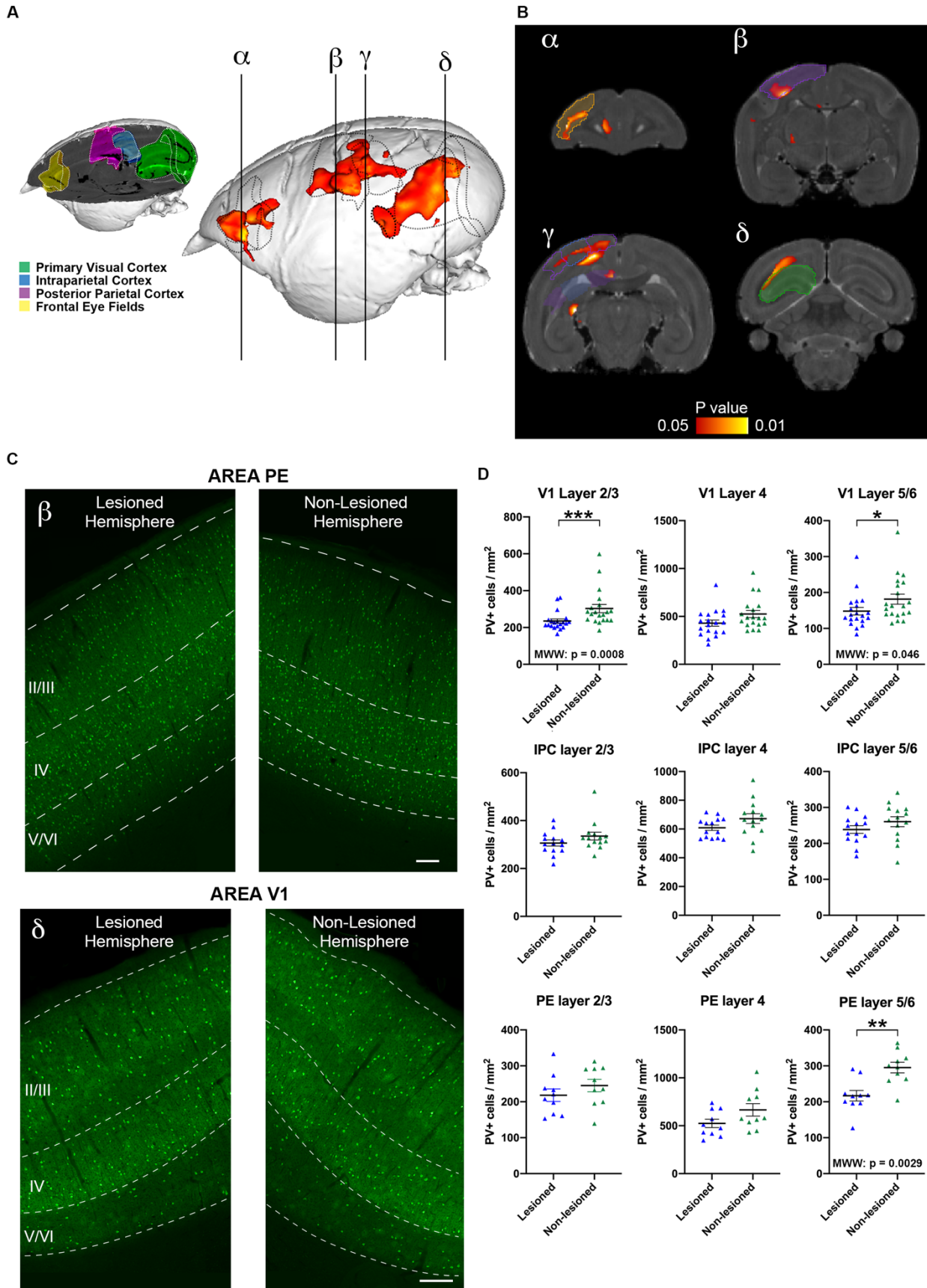
33

34 **Early-life lesions of MT lead to widespread changes in cortical architecture**

35 An advantage of our early-life lesion model is that it allows us to perform longitudinal MR
36 imaging following the lesion. We performed whole brain DTI scans on our lesioned animals at 36
37 weeks to determine the extent of chronic disruption to the cortical architecture. Voxel based
38 morphometric (VBM) analysis of the DTI maps between the lesioned and non-lesioned
39 hemisphere revealed, a reduction in fractional anisotropy (FA) in the intraparietal cortical areas
40 AIP, MIP, posterior parietal area PE (dorsal stream areas), the frontal eye fields (FEFs) and V1 (p
41 value <0.05)(**Fig. 1A; Fig. 4A, B**), areas MT has strong monosynaptic connections with. This
42 result is suggestive of an altered state in the neuroanatomy of these areas, where a reduction in
43 FA, has been correlated with both axonal and grey matter damage(37, 38).

44
45 As we had previously demonstrated, there is a correlation between changes in FA and
46 remodelling of the local circuitry(39), therefore we examined more closely the cellular
47 neuroanatomy in the areas affected by the lesion of MT. Specifically, quantification of the
48 calcium-binding protein, parvalbumin (PV) positive interneurons was undertaken as PV+ neurons
49 have garnered significant interest as a component in the maturation of the neocortex and are
50 functionally capable of amplifying circuit function(40–42). When compared to the non-lesioned
51 hemisphere, PV+ cell density within the ipsilesional hemisphere was reduced in V1 (Mann-
52 Whitney U test. Layers 2/3, p value = 0.0008; layers 5/6, p value = 0.046) and PE (Mann-Whitney
53 U test. Layers 5/6, p value = 0.0029)(**Fig 4C, D**). Although there was a reduction in of PV+ cells
54 in the other layers of V1 and PE, as well as IPC in the lesion animals, these were not significant.

55



57 **Figure 4. Microstructural changes to the cortex following a unilateral MT lesion, as revealed**
58 **by Diffusion Tractography Imaging (DTI) and parvalbumin (PV) fluorescent**
59 **immunohistochemistry.**

50

51 **(A)** Voxel-based morphometry of fractional anisotropy (FA) maps. Yellow-red clusters represent
52 significant hemispheric differences in FA, which was lower and observed in the ipsi-lesional
53 primary visual cortex, intraparietal cortex, posterior parietal cortex and frontal eye fields (Left vs
54 Right, n=5). Vertical lines (α , β , γ , δ) represent coronal sections in **(B)**. **(C, D)** PV+ interneurons
55 were reduced in the lesioned hemisphere of areas PE and V1 (scale bar = 200 μ m). Scatter plots
56 show significant reduction in PV neuronal density in infragranular layers of PE (p value = 0.0029)
57 as well as supragranular layers (p value = 0.0008) and infragranular layers (p value = 0.046) of
58 V1.

59

70 **Discussion**

71 This study was conceived with the objective to determine how MT contributes to development of
72 the dorsal stream. Further, an early-life unilateral lesion of MT would enable us to determine the
73 lifelong behavioural deficits associated with loss of this central area of the dorsal stream and the
74 impact this has on upstream and downstream cortices. Clinical studies which examined the
75 consequence of losing V1 in early life vs adulthood demonstrated a marked difference in
76 behavioural performance(26–28). Patient BI, whom suffered a bilateral V1 injury at nine days of
77 age retains the ability to perceive colour and possesses significant conscious vision. When
78 comparing the visual abilities of BI to an extensively studied blindsight patient, such as GY, who
79 sustained an injury to V1 at the age of 8, BI possesses greater preservation of vision. As there is a
80 strong correlation with the age of when an injury is acquired and the preservation of abilities that
81 neuroplasticity affords, we wanted to explore the effects an MT lesion would have on visuomotor
82 behaviour in a developing visual system. Additionally, we wanted to determine if there are
83 behaviours and brain areas which critically depend on MT. From our results, it is clear that an
84 early-life lesion of MT has a significant impact on visual system behaviour and architecture and
85 provides evidence that area MT is crucial in the normal establishment of the dorsal stream
86 network.

87
88 Seminal works studying the effect of lesions to MT on visual behaviour have unfortunately only
89 looked at adult acquired loss. Newsome and colleagues provided awake behavioural evidence in
90 the macaque that sensitivity to motion coherence is significantly disrupted following lesion to
91 MT(43). Furthermore, MT is required to accurately track moving stimulus with smooth pursuit
92 eye saccades. Visuomotor behaviour following bilateral MT lesion in adulthood has been
93 examined in the macaque(44). The subjects were presented a battery of tests to probe reach and
94 grasp behaviour in static and moving objects. Most notably, MT lesioned animals showed

95 impairment in their ability to engage in a static reach and grasp task whereby the food reward is
96 placed in a narrow slot so that the animal must only use the index and thumb for successful
97 retrieval of the food reward. Closer examination of the retrieval mechanism employed by the
98 adult MT-lesion animals showed they had difficulty in orientating their hand and typically had to
99 grasp the food reward with their whole hand and were unable to exhibit fine grasps with their
100 fingertips. The authors were unable to determine the impact the adult acquired bilateral MT loss
101 would have on visuomotor behaviour in moving objects. The moving object retrieval task in their
102 study consisted of a spinning bowl which would rotate at 240RPM. A banana pellet would be
103 dropped in the spinning bowl and as such bounce around. All animals had difficulty with this task
104 and no significant difference was observed between control and lesioned cohorts. In our study,
105 our animals also showed perturbations in hand posture when engaging in the static task as seen
106 with MT lesioned animals, exhibiting a larger MGA when reaching for food reward. This
107 suggests that MT is required for prehension throughout life. However, it is possible that the
108 deficits observed in this adult lesion model are due to the lesion extending beyond MT, as
109 removal of underlying white matter was a component of the ablation and degeneration of the
110 LGN observed, suggestive of damage to the optic radiation.

11
12 Clinically, there has only been one case of cerebral motion blindness described. Patient LM
13 suffered a bilateral vascular insult to the temporal portions of her brain in adulthood, which
14 included MT, as an adult with no injury evident in V1(23). Visual assessment of patient LM
15 demonstrated that she had perturbations in reach and grasp behaviour, oculomotor scanning
16 patterns and significant impairment in perceiving moving stimulus, although her ability to
17 discriminate the colour and form of objects remained normal(24, 45). While LM clearly had
18 akinetopsia, she demonstrated an ability to reach and grasp static objects, and objects which

19 moved up to speeds of 0.5m/sec (46). At speeds greater than 0.5m/sec, her performance greatly
20 diminished and often executed her reach with greater velocity.

21

22 Our results share certain similarities with what has been observed in LM. Early-life MT lesioned
23 marmosets also performed poorly when intercepting moving objects and displayed greater peak
24 velocity and acceleration in their executed reach compared to controls during the static task. A
25 notable difference between our study and LM's capabilities is that LM performed remarkably
26 well when reaching for objects that were static or slower than 0.5m/sec and her ability to intercept
27 objects at low speeds was on par with that of controls. Clinically, there is evidence that even with
28 static object retrieval, transcranial magnetic stimulation of MT interferes with fluid goal-directed
29 reaching(47). Our early-life lesioned marmosets, as well as the macaques with adulthood lesions
30 in MT in the Gattass and colleagues' study, were unable to replicate the success LM possesses
31 with static object retrievals. We believe LM's ability to reach out to stationary and slow-moving
32 stimuli could be a testament to her remarkable adaptive strategies in utilising the static visual cues
33 available to her to estimate trajectories of slow-moving items and her hand relative to the
34 stationary target object. As the marmosets in our study displayed impairment in retrieval of
35 moving objects akin to patient LM, we postulate that the plasticity of the developing brain does
36 not permit for recovery of visuomotor function in moving targets. As such MT serves a critical
37 node for visuomotor behaviours which require information from moving stimulus throughout life.

38

39 Further dissection of the failed behavioural trials by each marmoset in the moving object task
40 revealed that the lesioned cohort initiated the reach prematurely. This observed behaviour could
41 be due to the animal's inability to accurately detect the speed of the moving stimulus -
42 akinetopsia, a deficit which was also observed in LM. It should be noted that motion is encoded in
43 multiple cortical areas and not just MT(48, 49). Therefore, the intrinsic ability of the brain to

44 translate motion perception into a meaningful and precise goal-directed action relies on more than
45 just sensitivity to motion coherence and further reinforces how integral MT is for object
46 interaction, and the integral role it must place in the establishment of the associated networks
47 during development.

48
49 Existing literature has highlighted the importance the medial intraparietal area (MIP) and parietal
50 area (PE) serve in reaching actions and limb coordination(50, 51). Considering we observed
51 anatomical alterations specifically in these areas following an early-life lesion of MT, we suggest
52 they are complicit in the perturbed reaching behaviour observed in both the static and moving
53 object tasks. However, this does not explain why the lesioned marmosets demonstrate a similar
54 kinematic profile as their control counterparts when intercepting moving targets. It is most likely,
55 as marmosets do not have a refined hand use akin to macaques or chimpanzees(52, 53), that the
56 tendency to execute reach and grasp tasks on moving targets with maximum velocity is their
57 natural teleological behaviour, especially for fast arboreal manoeuvres. Despite the comparable
58 kinematics in the moving object task, ultimately the lesioned animals tended to prematurely reach
59 and fail to collect moving object.

50
51 To the best of our knowledge, this is the first study examining the tuning properties of V1 neurons
52 following an early-life injury to an extrastriate area. Previously, studies have examined the
53 physiological properties of neurons in MT following a lesion of V1(54, 55), revealing receptive
54 field size and tuning properties were dramatically affected. However, MT responses remained
55 robust and largely unaffected following V1 lesions sustained in early life(56). The only noticeable
56 deficit was a reduced proportion of DS neurons. This supports the idea that the visual brain is
57 largely able to execute contingency mechanisms during development to afford a higher level of
58 functional recovery following the early-life loss of V1. This concept has also been observed

59 clinically in subject BI, who following a bilateral early-life injury to V1 has significant
70 preservation of vision, including sensitivity to moving stimuli(27). We wanted to observe the
71 converse; if the tuning properties of V1 are vulnerable during development and extent of co-
72 dependency between V1 and MT to develop DS or any other tuning property. In this study, we
73 observed no dramatic perturbations in the tuning properties of V1 neurons. We did observe a
74 lower proportion of DS neurons, which parallels previous findings for MT following an early-life
75 lesion of V1(56). Modifications of V1 tuning properties, such as DS or even orientation
76 selectivity has been reported before(57–59) but none specifically in relation to V1-MT circuitry.
77 This warrants further investigation to determine if the MT-V1 projection serves a role in early life
78 to tune DS within V1 neurons.

79
80 As PV interneurons form the majority of GABAergic interneurons in V1(60), we sought to
81 determine if there were disruptions to the local circuits by quantifying PV+ interneurons. Further,
82 it is well documented that the local interneuron circuitry is more susceptible during development
83 than in adulthood(61). MT has considerable reciprocal connectivity with layers 3C and 6 of
84 V1(5),and we revealed a reduced PV+ cell density within both supra and infragranular layers.
85 PV+ neurons in V1 have a diversity of feature-specific visual responses that include sharp
86 orientation and DS, small receptive fields, and bandpass spatial frequency tuning(62). These
87 results suggest that subsets of parvalbumin interneurons are components of specific cortical
88 networks, and that perisomatic inhibition contributes to the generation of precise response
89 properties. Ablation of PV in V1 interneurons has previously been observed to decrease DS
90 properties within V1(63). Therefore, it is conceivable that the reduced PV population in V1
91 following the early-life lesion of MT is the underlying basis to our observation of a lower
92 proportion of DS neurons in V1.

04 The implications of this current study extend our understanding of the central role area MT
05 occupies in the early establishment of the dorsal stream and associated behaviours, and its role as
06 an anchor in the developing visual cortex. Further, our observation of a lower proportion of DS
07 neurons within V1 could suggest a level of dependency on MT in early life in the tuning and
08 appropriate maturation of V1 neurons. While marmosets lack fine motor skills, they have
09 demonstrated their ability to use tools(64) and have the circuitry for accurate reach and grasp
10 behaviours. Teleologically, the early establishment of the dorsal stream network provides
11 primates the capacity to process vision-for-action, including accurate reaching and grasping
12 behaviour, which is integral to their survival.

03

04

05

06 **Materials and Methods**

07

08 ***Subjects***

09 Five New World marmoset monkeys (*Callithrix jacchus*) received a mechanical ablation of the
10 middle temporal (MT) area at postnatal day (PD) 14 (**Table 1**). Following surgical ablation, the
11 animals were allowed 12 months of recovery before undergoing training for visual behaviour
12 experimentation. Three aged-matched animals were used as controls for behavioural experiments
13 (Table 1). All experiments were conducted in accordance with the Australian Code of Practice
14 for the Care and Use of Animals for Scientific Purposes. All procedures were approved by the
15 Monash University Animal Ethics Committee, which also monitored the health and wellbeing of
16 the animals throughout the experiments.

<i>Animal ID</i>	Neonatal unilateral MT Ablation	MRI/DTI	Reach & Grasp Behaviour	V1 Electrophysiology	Immuno-histochemistry
<i>M1695</i>	X	X		X	
<i>F1696</i>	X	X		X	
<i>F1992</i>	X	X			X
<i>F2019</i>	X	X	X		X
<i>F2020</i>	X	X	X		X
<i>F1565</i>			X		
<i>F1575</i>			X		
<i>M2086</i>			X		

17 **Table 1** - Marmosets employed in current study. Prefixes in animal ID: M=male; F=female.

18 **Mechanical ablation of area MT**

19 Neonatal marmosets (PD 14; n=5) were anaesthetised with isoflurane (1-2% in medical oxygen at
20 0.5L.min⁻¹) and placed into a custom built non-ferromagnetic stereotaxic frame to facilitate T2-
21 weighted MRI to allow for demarcation and targeted ablation of area MT (**Fig. 1B**). Full details of
22 preparation of the animal and how to localise areas of interest with MRI guidance have been
23 described previously(65). Scans were exported as DICOM files and the brain images were
24 visualised on the Horos v3.3.5 software (<https://horosproject.org>). Once MT was visualised,
25 ablations were performed using a biopsy punch (diameter = 3.0 mm). Following ablation of
26 cerebral tissue, the cavity was filled with Gelfoam, the cranium was reconstructed and the scalp
27 was sutured. Animals would receive post-surgical antibiotic and analgesic medication and then
28 allowed a minimum of 12 months recovery. to allow for plastic reorganisation of the brain.

29

30 **Longitudinal MR imaging**

31 During the animal's recovery, structural T2 images were acquired on a 9.4T small-bore animal
32 scanner (Agilent) 6 weeks and 36 weeks post lesion to identify the extent of the lesion (**Fig. 1B**).
33 The parameters for the T2 scan are: MRI structural images comprised T2 weighted images (9.4
34 Tesla 18 cm bore MRI scanner (Bruker); 2D-RARE sequence, TR=12000 ms, TE=48 ms, Matrix
35 size=200x180, FOV= 40x36mm², number of slices = 80, slice thickness=0.4mm, RARE factor =
36 8, axial plane, and 4 averages; scan time 30 minutes). Additionally, at the same time points,
37 diffusion tensor imaging (DTI) was acquired for analysis of changes in microstructure in visual
38 cortical tissue following injury. DTI was acquired in the axial orientation using a six-shot spin-
39 echo echo planar imaging (EPI)- based DTI sequence. Scan parameters included: TR/TE of
40 3,000/31 ms, FOV of 38.4 × 38.4 mm², data matrix of 96 × 96, and 50 slices with thickness of 0.4
41 mm. Diffusion encoding gradients were applied in 30 directions, with a b value of 800, gradient
42 duration of 5 ms, and separation of 18 ms. A reference scan with inverted phase and readout

43 gradients was acquired for phase correction to reduce EPI and DTI-specific artefacts. The average
44 of the reference and the original scan also increased the signal-to-noise ratio (SNR). The DTI
45 sequence was repeated four times and saved separately with the aim of further increasing SNR
46 and generating backup data in case any unexpected motion artifacts occurred during the relatively
47 long scan. The whole DTI scan took ~80 min.

48
49 Diffusion weighted data were pre-processed and analysed using tools from different software
50 packages that work well with the small sized marmoset brain. MriCron, dcm2nii script
51 (<http://people.cas.sc.edu/rorden/mricron/dcm2nii.html>) was used for conversion of DiCOM to
52 nifti files; averaging, orientation of different DWI repetitions and corrections for movement
53 distortions was scripted using FSL 5.0.9 software library of the Centre for Functional Magnetic
54 Resonance Imaging of the Brain (FMRIB, University of Oxford, UK, www.fmrib.ox.ac.uk/fsl).
55 Binary brain masks were generated using Brainsuite 15c (www.brainsuite.org). Diffusion tensors
56 and derived fractional anisotropy maps (FA) were calculated using MRtrix3 (www.mrtrix.org).

57 (66)

58

59 **Visual Behaviour Training**

50 Visual behaviour experiments commenced following a minimum of 12 months recovery from the
51 MT ablative surgery. Detailed stepwise training and habituation protocols to allow for
52 implementing reach and grasp behavioural experiments in the marmoset have been previously
53 described(32).

54

55 Animals were first trained to enter a custom fabricated behaviour training box (Monash
56 Instrumentation Development Facility). Food rewards are given to positively encourage
57 participation in desired behaviours. Following habituation with the behaviour box, the animal is

58 transferred to an adjacent room where the behavioural experimentation is conducted. Food
59 rewards are once again given to habituate the animal with the room.
70
71 Following complete habituation, the animal's ability in goal orientated reach and grasp of static
72 objects was examined whereby the animal is presented with a target object in the form of a food
73 reward (piece of fruit). The food reward was placed in one of two positions on a pedestal, both of
74 which are equidistant to an aperture in the behaviour box (**Fig. 2A-D**). These two positions could
75 favour either the left or right hand. To determine the animals' hand preshaping behaviour and if
76 the size of the target object would have a significant effect on performance, the food reward was
77 cut into cuboids where the largest face would be ~5x5mm or ~10x10mm. The precise size of the
78 food reward was qualified during the video analysis of each trial with in- built tools in Tracker
79 software. Before commencement of a static task trial, a blind is placed in front of the transport
80 box and its apertures so the animal could not prime its hand in anticipation of the position of the
81 reward. Each static object retrieval session consisted of 15 - 20 trials. The proportion of trials of
82 small vs large object presentation was equal.

83
84 To assess the animal's ability in reaching and grasping a moving object, a single sized food
85 reward (cuboid, ~10x10mm face) was placed on the edge of a custom-built rotating turntable
86 ($\varnothing=14\text{cm}$, Monash University Instrumentation Development Facility)(**Fig. 2b, D**). The centre of
87 the turntable was aligned with the centre of the transport which was equidistant to both right and
88 left apertures. Objects were always placed in the same spot of the turntable across all trials.
89 Shutters were used to occlude the reaching apertures to control the use of hand (i.e, the animal
90 would use its right hand when the right aperture was unblocked and vice versa). The shutter was
91 removed, and the trial commenced once the food reward had undergone one revolution to ensure
92 that the turntable can accelerate to the desired speed for the task. Animals were given a 10-second

03 response time for each trial. Animals were allowed a maximum of three attempts within each trial
04 for it to be considered successful. Background white noise was played throughout the sessions to
05 minimise any impact the noise produced by the turntable would have in the animal's performance.
06 Three independent variables were incorporated to the turntable task; 1) Six different revolution
07 speeds, which ranges from 10 to 60 revolutions per minute (RPM), 2) Direction of the revolution
08 (clockwise/anti-clockwise), and 3) Hand used to retrieve the object (**Table 2**). This resulted in 24
09 different conditions that would be presented during a training session. The order of the trial
10 conditions randomised across sessions and a single condition (eg. object moving at a speed of
11 30RPM in a clockwise direction with the aperture opened for the left hand) did not repeat in the
12 same session.

03

Independent Variable	Description
Speed	10, 20, 30, 40, 50, 60 RPM
Direction	clockwise or anti-clockwise
Hand Use	Aperture blocked to allow for only the left or right hand for object retrieval

04 **Table 2** – Independent variables employed in moving reach and grasp task

05 **Analysis of visual behaviour performance**

06 Trials for the static object task were binned into three main categories; a successful trial was
07 defined as a single coordinated motor action to retrieve the object. Corrected trials occurred when
08 animals required fewer than three corrections in either their reach or grasp to retrieve the object

09 successfully. Failure to meet the conditions of the two previous bins, or not completing the action
10 within the given time frame, was assigned to the failed trial category. Trials for the moving object
11 task were binned into two main categories; a successful trial when the animal retrieved the
12 rotating object within three attempts, a failed trial when more than three attempts were required
13 for retrieval or the object was dislocated from the initial position. Trials with no response were
14 considered invalid and discarded.

15 All trials were recorded using “GoPro HERO4 Black” camera (1280x790-pixel resolution, 120
16 frames/sec, narrow view) from the transverse plane perpendicular to the plane of motion (i.e. top-
17 down view) and videos captured were analysed offline. The same investigator (C-K.C) performed
18 and analyzed all videos offline manually in a blinded manner to determine the performance and
19 kinematics of each trial. The performance as expressed by error rate was determined by dividing
20 the number of failed trials over the total number of trials within a given session. The overall
21 performance of a given task in each animal was determined with permutation testing of the
22 performance of all sessions.

23 Video files were transferred to an open source software Tracker v4.93 (physlets.org/tracker/)
24 designed to perform a 2D kinematic analysis. A reference scale of known size remained in the
25 field of view and was positioned at the height of the reaching movements to eliminate any
26 perspective errors. The edges of the reaching platform served as reference points for X and Y axes
27 to track movement trajectories across each trial. Three metrics were measured in the video
28 analysis. The maximum grip aperture (MGA) between the animal’s thumb and index finger when
29 the animal pre-shapes its hand in acquiring an object, the velocity at which the animal would
30 move to grasp an object as well as the acceleration. Additionally, the junctions between the nail
31 and digit of the index finger and thumb were used as reference points to measure the Euclidean
32 distance over time. Movement duration was defined as the time elapsed from the moment the
33 thumb reference point was visible outside of the reaching aperture in the box to the moment when

34 either the index finger or thumb made contact with piece of fruit (identified by it moving for at
35 least three consecutive frames). The length of the food reward in each trial was measured against
36 the reference scale and plotted against the MGA of the trial using Prism version 8.4.2 to
37 determine if the animal exhibited any hand preshaping behaviour. All failed trials were further
38 sorted to determine whether the animals exhibited a premature or delayed reach while attempting
39 to retrieve the food reward. The angle between the final hand position over the turntable and the
40 food reward was then measured on Tracker v4.93 to determine the accuracy of targeting the
41 object (**Fig. 2I**). Mean angulation was calculated in each session for each animal to reveal overall
42 angulation of failed trials across all sessions. $P \leq 0.05$ were considered to be statistically
43 significant. All data are presented as mean \pm standard error of the mean SEM).

44

45 **Electrophysiological recordings**

46 Animals M1695 and F1696 underwent a single recording session under deep anaesthesia. The
47 detailed methodology of how the animals were prepared for electrophysiology is described in
48 Bourne & Rosa(67). In brief, animals underwent a tracheotomy and two craniotomy procedures
49 with anaesthesia being maintained with a continuous intravenous infusion of a mixture of
50 pancuronium bromide ($0.1 \text{ mg.kg}^{-1}.\text{h}^{-1}$), sufentanil ($6 \mu\text{g.kg}^{-1}.\text{h}^{-1}$), and dexamethasone (0.4
51 $\text{mg.kg}^{-1}.\text{h}^{-1}$), in a saline–glucose solution. During the recordings, animals were also ventilated
52 with nitrous oxide and oxygen (7:3).

53

54 The electrophysiological experiments consisted of two phases. Firstly, the scotoma of each animal
55 was mapped by determination of MT complex receptive fields along the perimeter of the lesion
56 core. Following identification of the scotoma, recordings were conducted in V1 within and
57 outside the lesion projection zone. Recordings were performed with tungsten microelectrodes (\sim
58 $1\text{M}\Omega$). Insertion of the electrodes to our eccentricity of interest was guided by stereotaxic and

59 topographical data described in previous studies(5, 68) . Amplification and filtering were
60 achieved via an AM Systems model 1800 microelectrode alternating current amplifier. Stimuli
61 presentation and methods for quantification of tuning for orientation and direction as well as
62 spatial and temporal frequency within V1 was performed as per previous studies(35, 56, 69).

53

54 **Histology and immunohistochemical tissue processing**

55 Animals were euthanised with an overdose of sodium pentobarbitone (>100mg/kg) then
56 transcardially perfused with 10mM PBS that has been supplemented with heparin (50 IU/ml of
57 PBS), followed by 4% paraformaldehyde in 10mM PBS. Brains were post-fixed in 4%
58 paraformaldehyde then dehydrated in serial solutions of PBS-sucrose before being snap frozen in
59 2-methylbutane that has been chilled to -50°C and stored in a -80°C freezer until cryosectioning.

70

71 Brain samples were cryosectioned in the coronal plane at 50um, divided into five series and
72 stored free-floating in a cryoprotective solution (as outlined in previous work(3)).

73 Half a series was stained for myelin via silver impregnation(70) to demarcate area MT and to
74 qualify the size of the lesion and spatially, the extent of MT which was ablated (**Fig. 1C**). Free-
75 floating sections were labelled with GABAergic interneuronal marker parvalbumin (PV; Swant,
76 PV27 1:3000).

77

78 **Microscopy and digital image processing**

79 Brain sections were imaged with an Axio Imager Z1 microscope (Zeiss). Images were obtained
80 with a Zeiss Axiocam HRm digital camera using Axiovision software (v. 4.8.1.0) at a resolution
81 of 1024 by 1024 or 2048 by 2048 pixels and saved in ZVI and exported to TIFF format. The
82 objectives used were Zeiss EC-Plan Neofluar 5x0.16, #420330- 9901, EC-Plan Neofluar 10x0.3,
83 #420340-9901. Filter sets used for visualizing immunolabelled cells were Zeiss 38 HE eGFP #

34 489038-9901-000.

35 Images used for cell density quantification were taken with the 10x objective. Stitching of images
36 and adjustments to contrast and brightness was performed using Adobe Photoshop 2020 v21.0.1
37 or Zeiss MosaiX software. The contours, boundaries, and line art of all figures were drawn using
38 Adobe Illustrator 2020 v24.0.1.

39 Quantification of interneuronal density was conducted as per previous work(30). Each area or
40 interest had analysis of PV cell density within the supragranular layers 2 and 3, granular layer 4 or
41 infragranular layers 5 and 6. For each animal, 6 sections randomly selected across the anterior-
42 posterior axis across our areas of interest. The regions that were sampled are V1, the areas around
43 the intraparietal area which consists of areas AIP, LIP & MIP and area PE which is part of the
44 posterior parietal cortex. Analysis of photomontages of CB and PV IR cells was conducted using
45 Fiji image software(71). The same investigator (W.C.K) performed all quantifications in a blinded
46 manner.

47

48 **Statistical analysis**

49 Assessment of the behavioural performance of an animal was determined through their error rate
50 in each session. The error rate, as well as the frequency of successful retrieval on the first attempt
51 was examined using a non-parametric permutation test on Microsoft Excel version 16.62. The
52 kinematic analysis of reach and grasp behaviours which include MGA, velocity, acceleration and
53 angulation was also examined using a non-parametric permutation test on Microsoft Excel
54 version 16.62. Within the permutation test, data were repeatedly resampled (5000 times) to
55 determine the difference between cohorts. $P \leq 0.05$ were considered to be statistically significant.

06 To determine if sizes of the food reward have any influence on the performance, an ANCOVA
07 analysis was performed on Prism version 8.4.2 to compare the error rate of large and small sizes
08 across sessions. A linear regression was also performed on Prism version 8.4.2 to determine the
09 hand preshaping behaviour against food lengths. $P \leq 0.05$ were considered to be statistically
10 significant.

11 Statistical analysis for PV+ cell density as presented as mean \pm standard error of the mean was
12 carried out using Prism version 8.4.2 software. Comparison between the ipsi-lesional and contra-
13 lesional V1 were examined by a non-parametric Mann-Whitney U test. $P \leq 0.05$ were considered
14 to be statistically significant.

15 For voxel-based morphometry statistical analysis of FA maps a general linear model following a
16 two-sample t-test was used comparing left (lesioned) and right (control) hemispheres (SPM12,
17 The Wellcome Trust Centre for Neuroimaging, UCL, UK) as follows. FA maps from all MT-
18 lesion animals were registered to a marmoset brain template
19 (<http://brainatlas.brain.riken.jp/marmoset/>. BSI-Neuroinformatics, Riken Institute, Japan) using
20 the normalized mutual information function (7-degree B-spline). Resulting images were smoothed
21 with 1 mm isotropic Gaussian kernel. Subsequently, images were flipped and registered again to
22 original unflipped images. Significance level was $P < 0.05$ corrected for the familywise error rate
23 (FWE) with and extended threshold of 1 voxel. Z-scores converted to P values were displayed on
24 the Brain/MINDS 3D digital marmoset atlas(66) using Mango 4.1 software from the Research
25 Imaging Institute, University of Texas Health Centre at San Antonio (ric.uthscsa.edu/mango).

26

27 **References**

28

29 1. M. A. Goodale, A. D. Milner, Separate visual pathways for perception and action. *Trends*
30 *Neurosci.* **15**, 20–25 (1992).

31 2. L. Ungerleider, M. Mishkin, Two cortical visual systems. In “Analysis of Visual Behavior”(DJ
32 Ingle, MA Goodale, and RJW Mansfield, eds.). *null* (1982).

33 3. J. A. Bourne, M. G. P. Rosa, Hierarchical Development of the Primate Visual Cortex, as
34 Revealed by Neurofilament Immunoreactivity: Early Maturation of the Middle Temporal Area
35 (MT). *Cereb Cortex.* **16**, 405–414 (2005).

36 4. C. E. Warner, W. C. Kwan, J. A. Bourne, The early maturation of visual cortical area MT is
37 dependent on input from the retinorecipient medial portion of the inferior pulvinar. *Journal of*
38 *Neuroscience.* **32**, 17073–17085 (2012).

39 5. I.-C. Mundinano, W. C. Kwan, J. A. Bourne, Retinotopic specializations of cortical and
40 thalamic inputs to area MT. *Proc National Acad Sci.* **116**, 23326–23331 (2019).

41 6. L. C. Sincich, K. F. Park, M. J. Wohlgemuth, J. C. Horton, Bypassing V1: a direct geniculate
42 input to area MT. *Nat Neurosci.* **7**, 1123–1128 (2004).

43 7. C. E. Warner, Y. Goldshmit, J. A. Bourne, Retinal afferents synapse with relay cells targeting
44 the middle temporal area in the pulvinar and lateral geniculate nuclei. *Front Neuroanat.* **4**, 8–8
45 (2010).

46 8. M. G. P. Rosa, Visual maps in the adult primate cerebral cortex: some implications for brain
47 development and evolution. *Braz J Med Biol Res.* **35**, 1485–1498 (2002).

- 48 9. L. G. Ungerleider, M. Mishkin, The striate projection zone in the superior temporal sulcus
49 of *Macaca mulatta*: Location and topographic organization. *J Comp Neurology*. **188**, 347–366
50 (1979).
- 51 10. D. C. Lyon, J. H. Kaas, Connectional and Architectonic Evidence for Dorsal and Ventral V3,
52 and Dorsomedial Area in Marmoset Monkeys. *J Neurosci*. **21**, 249 (2001).
- 53 11. J. Maunsell, D. van Essen, The connections of the middle temporal visual area (MT) and their
54 relationship to a cortical hierarchy in the macaque monkey. *J Neurosci*. **3**, 2563–2586 (1983).
- 55 12. L. A. Krubitzer, J. H. Kass, Cortical connections of MT in four species of primates: Areal,
56 modular, and retinotopic patterns. *Visual Neurosci*. **5**, 165–204 (1990).
- 57 13. C. L. Colby, J. R. Duhamel, M. E. Goldberg, Ventral intraparietal area of the macaque:
58 anatomic location and visual response properties. *J Neurophysiol*. **69**, 902–914 (1993).
- 59 14. M. G. Maioli, S. Squatrito, C. Galletti, P. P. Battaglini, E. R. Sanseverino, Cortico-cortical
50 connections from the visual region of the superior temporal sulcus to frontal eye field in the
51 macaque. *Brain Res*. **265**, 294–299 (1983).
- 52 15. P. Majka, S. Bai, S. Bakola, S. Bednarek, J. M. Chan, N. Jermakow, L. Passarelli, D. H.
53 Reser, P. Theodoni, K. H. Worthy, X.-J. Wang, D. K. Wójcik, P. P. Mitra, M. G. P. Rosa, Open
54 access resource for cellular-resolution analyses of corticocortical connectivity in the marmoset
55 monkey. *Nat Commun*. **11**, 1133 (2020).
- 56 16. C.-S. Lin, J. H. Kaas, Projections from the medial nucleus of the inferior pulvinar complex to
57 the middle temporal area of the visual cortex. *Neuroscience*. **5**, 2219–2228 (1980).

- 58 17. D. C. Lyon, J. J. Nassi, E. M. Callaway, A Disynaptic Relay from Superior Colliculus to
59 Dorsal Stream Visual Cortex in Macaque Monkey. *Neuron*. **65**, 270–279 (2010).
- 70 18. L. G. Ungerleider, R. Desimone, T. W. Galkin, M. Mishkin, Subcortical projections of area
71 MT in the macaque. *J Comp Neurology*. **223**, 368–386 (1984).
- 72 19. R. Dubner, S. M. Zeki, Response properties and receptive fields of cells in an anatomically
73 defined region of the superior temporal sulcus in the monkey. *Brain Research*. **35**, 528–532
74 (1971).
- 75 20. T. D. Albright, Direction and orientation selectivity of neurons in visual area MT of the
76 macaque. *J Neurophysiol*. **52**, 1106–1130 (1984).
- 77 21. W. Newsome, R. Wurtz, M. Dursteler, A. Mikami, Deficits in visual motion processing
78 following ibotenic acid lesions of the middle temporal visual area of the macaque monkey. *J*
79 *Neurosci*. **5**, 825 (1985).
- 80 22. M. R. Dürsteler, R. H. Wurtz, W. T. Newsome, Directional pursuit deficits following lesions
81 of the foveal representation within the superior temporal sulcus of the macaque monkey. *Journal*
82 *of Neurophysiology*. **57**, 1262–1287 (1987).
- 83 23. J. Zihl, D. V. Cramon, N. Mai, Selective Disturbance of Movement Vision After Bilateral
84 Brain Damage. *Brain*. **106**, 313–340 (1983).
- 85 24. S. Zeki, Cerebral Akinetopsia (Visual Motion Blindness). *Brain*. **114**, 811–824 (1991).
- 86 25. A. K. JANSEN-AMORIM, B. LIMA, M. FIORANI, R. GATTASS, GABA inactivation of
87 visual area MT modifies the responsiveness and direction selectivity of V2 neurons in Cebus
88 monkeys. *Visual Neurosci*. **28**, 513–527 (2011).

- 39 26. L. Weiskrantz, E. K. Warrington, M. Sanders, J. Marshall, Visual capacity in the hemianopic
90 field following a restricted occipital ablation. *Brain*. **97**, 709–728 (1974).
- 91 27. I.-C. Mundinano, J. Chen, M. de Souza, M. G. Sarossy, M. F. Joannis, M. A. Goodale, J. A.
92 Bourne, More than blindsight: Case report of a child with extraordinary visual capacity following
93 perinatal bilateral occipital lobe injury. *Neuropsychologia*. **128**, 178–186 (2019).
- 94 28. S. E. Leh, A. Ptito, M. Schönwiesner, M. M. Chakravarty, K. T. Mullen, Blindsight Mediated
95 by an S-Cone-independent Collicular Pathway: An fMRI Study in Hemispherectomized Subjects.
96 *J Cognitive Neurosci*. **22**, 670–682 (2009).
- 97 29. A. Tran, M. W. MacLean, V. Hadid, L. Lazzouni, D. K. Nguyen, J. Tremblay, M. Dehaes, F.
98 Lepore, Neuronal mechanisms of motion detection underlying blindsight assessed by functional
99 magnetic resonance imaging (fMRI). *Neuropsychologia*. **128**, 187–197 (2019).
- 00 30. I.-C. Mundinano, W. C. Kwan, J. A. Bourne, Mapping the mosaic sequence of primate visual
01 cortical development. *Front Neuroanat*. **9**, 132 (2015).
- 02 31. C. E. Warner, W. C. Kwan, D. Wright, L. A. Johnston, G. F. Egan, J. A. Bourne, Preservation
03 of Vision by the Pulvinar following Early-Life Primary Visual Cortex Lesions. *Current Biology*.
04 **25**, 424–434 (2015).
- 05 32. D. M. Fox, I. Mundinano, J. A. Bourne, Prehensile kinematics of the marmoset monkey:
06 Implications for the evolution of visually-guided behaviors. *J Comp Neurol*. **527**, 1495–1507
07 (2019).
- 08 33. D. Rose, C. Blakemore, An analysis of orientation selectivity in the cat's visual cortex. *Exp*
09 *Brain Res*. **20**, 1–17 (1974).

- 10 34. G. H. Henry, P. O. Bishop, R. M. Tupper, B. Dreher, Orientation specificity and response
11 variability of cells in the striate cortex. *Vision Res.* **13**, 1771–1779 (1973).
- 12 35. H.-H. YU, M. G. P. Rosa, Uniformity and diversity of response properties of neurons in the
13 primary visual cortex: Selectivity for orientation, direction of motion, and stimulus size from
14 center to far periphery. *Visual Neurosci.* **31**, 85–98 (2014).
- 15 36. D. L. Ringach, R. M. Shapley, M. J. Hawken, Orientation Selectivity in Macaque V1:
16 Diversity and Laminar Dependence. *J Neurosci.* **22**, 5639–5651 (2002).
- 17 37. T. A. G. M. Huisman, L. H. Schwamm, P. W. Schaefer, W. J. Koroshetz, N. Shetty-Alva, Y.
18 Ozsunar, O. Wu, A. G. Sorensen, Diffusion tensor imaging as potential biomarker of white matter
19 injury in diffuse axonal injury. *Ajnr Am J Neuroradiol.* **25**, 370–6 (2004).
- 20 38. A. Shereen, N. Nemkul, D. Yang, F. Adhami, R. S. Dunn, M. L. Hazen, M. Nakafuku, G.
21 Ning, D. M. Lindquist, C.-Y. Kuan, Ex vivo diffusion tensor imaging and neuropathological
22 correlation in a murine model of hypoxia-ischemia-induced thrombotic stroke. *J Cereb Blood*
23 *Flow Metabolism Official J Int Soc Cereb Blood Flow Metabolism.* **31**, 1155–69 (2010).
- 24 39. I.-C. Mundinano, D. M. Fox, W. C. Kwan, D. Vidaurre, L. Teo, J. Homman-Ludiye, M. A.
25 Goodale, D. A. Leopold, J. A. Bourne, Transient visual pathway critical for normal development
26 of primate grasping behavior. *Proc National Acad Sci*, 201717016 (2018).
- 27 40. A. E. Hendrickson, J. F. M. van Brederode, K. A. Mulligan, M. R. Celio, Development of the
28 calcium-binding proteins parvalbumin and calbindin in monkey striate cortex. *J Comp Neurology.*
29 **307**, 626–646 (1991).

- 30 41. J. A. Cardin, M. Carlén, K. Meletis, U. Knoblich, F. Zhang, K. Deisseroth, L.-H. Tsai, C. I.
31 Moore, Driving fast-spiking cells induces gamma rhythm and controls sensory responses. *Nature*.
32 **459**, 663–667 (2009).
- 33 42. V. S. Sohal, F. Zhang, O. Yizhar, K. Deisseroth, Parvalbumin neurons and gamma rhythms
34 enhance cortical circuit performance. *Nature*. **459**, 698–702 (2009).
- 35 43. W. Newsome, E. Pare, A selective impairment of motion perception following lesions of the
36 middle temporal visual area (MT). *J Neurosci*. **8**, 2201 (1988).
- 37 44. R. Gattass, J. G. M. Soares, B. Lima, Effects of MT lesions on visuomotor performance in
38 macaques. *Prog Neurobiol*, 101931 (2020).
- 39 45. J. Zihl, C. A. Heywood, The contribution of LM to the neuroscience of movement vision.
40 *Frontiers Integr Neurosci*. **9**, 6 (2015).
- 41 46. T. Schenk, N. Mai, J. Ditterich, J. Zihl, Can a motion-blind patient reach for moving objects?
42 *Eur J Neurosci*. **12**, 3351–3360 (2000).
- 43 47. D. Whitney, A. Ellison, N. J. Rice, D. Arnold, M. Goodale, V. Walsh, D. Milner, Visually
44 Guided Reaching Depends on Motion Area MT+. *Cereb Cortex*. **17**, 2644–2649 (2007).
- 45 48. S. Pitzalis, M. I. Sereno, G. Committeri, P. Fattori, G. Galati, F. Patria, C. Galletti, Human
46 V6: The Medial Motion Area. *Cereb Cortex*. **20**, 411–424 (2009).
- 47 49. A. S. Tolias, G. A. Keliris, S. M. Smirnakis, N. K. Logothetis, Neurons in macaque area V4
48 acquire directional tuning after adaptation to motion stimuli. *Nat Neurosci*. **8**, 591–593 (2005).
- 49 50. L. H. Snyder, A. P. Batista, R. A. Andersen, Coding of intention in the posterior parietal
50 cortex. *Nature*. **386**, 167–170 (1997).

- 51 51. F. Filimon, J. D. Nelson, R.-S. Huang, M. I. Sereno, Multiple Parietal Reach Regions in
52 Humans: Cortical Representations for Visual and Proprioceptive Feedback during On-Line
53 Reaching. *J Neurosci.* **29**, 2961–2971 (2009).
- 54 52. M. CHIANG, Use of Tools by Wild Macaque Monkeys in Singapore. *Nature.* **214**, 1258–
55 1259 (1967).
- 56 53. C. Boesch, H. Boesch, Optimisation of Nut-Cracking With Natural Hammers By Wild
57 Chimpanzees. *Behaviour.* **83**, 265–286 (1983).
- 58 54. H. Rodman, C. Gross, T. Albright, Afferent basis of visual response properties in area MT of
59 the macaque. I. Effects of striate cortex removal. *J Neurosci.* **9**, 2033–2050 (1989).
- 60 55. J. H. Kaas, L. A. Krubitzer, Area 17 lesions deactivate area MT in owl monkeys. *Visual*
61 *Neurosci.* **9**, 399–407 (1992).
- 62 56. H.-H. Yu, T. A. Chaplin, G. W. Egan, D. H. Reser, K. H. Worthy, M. G. P. Rosa, Visually
63 Evoked Responses in Extrastriate Area MT after Lesions of Striate Cortex in Early Life. *J*
64 *Neurosci.* **33**, 12479 (2013).
- 65 57. F. Tretter, M. Cynader, W. Singer, Modification of direction selectivity of neurons in the
66 visual cortex of kittens. *Brain Res.* **84**, 143–149 (1975).
- 67 58. T. Pasternak, L. Leinen, Pattern and motion vision in cats with selective loss of cortical
68 directional selectivity. *J Neurosci.* **6**, 938–945 (1986).
- 69 59. A. Kohn, J. A. Movshon, Adaptation changes the direction tuning of macaque MT neurons.
70 *Nat Neurosci.* **7**, 764–772 (2004).

- 71 60. J. F. M. V. Brederode, K. A. Mulligan, A. E. Hendrickson, Calcium-binding proteins as
72 markers for subpopulations of GABAergic neurons in monkey striate cortex. *J Comp Neurology*.
73 **298**, 1–22 (1990).
- 74 61. F. V. Gomes, X. Zhu, A. A. Grace, Stress during critical periods of development and risk for
75 schizophrenia. *Schizophr Res*. **213**, 107–113 (2019).
- 76 62. S.-H. Lee, A. C. Kwan, S. Zhang, V. Phoumthippavong, J. G. Flannery, S. C. Masmanidis,
77 H. Taniguchi, Z. J. Huang, F. Zhang, E. S. Boyden, K. Deisseroth, Y. Dan, Activation of specific
78 interneurons improves V1 feature selectivity and visual perception. *Nature*. **488**, 379–383 (2012).
- 79 63. C. A. Runyan, J. Schummers, A. V. Wart, S. J. Kuhlman, N. R. Wilson, Z. J. Huang, M. Sur,
80 Response Features of Parvalbumin-Expressing Interneurons Suggest Precise Roles for Subtypes
81 of Inhibition in Visual Cortex. *Neuron*. **67**, 847–857 (2010).
- 82 64. Y. Yamazaki, C. Echigo, M. Saiki, M. Inada, S. Watanabe, A. Iriki, Tool-use learning by
83 common marmosets (*Callithrix jacchus*). *Exp Brain Res*. **213**, 63–71 (2011).
- 84 65. I.-C. Mundinano, P. A. Flecknell, J. A. Bourne, MRI-guided stereotaxic brain surgery in the
85 infant and adult common marmoset. *Nat Protoc*. **11**, 1299–1308 (2016).
- 86 66. A. Woodward, T. Hashikawa, M. Maeda, T. Kaneko, K. Hikishima, A. Iriki, H. Okano, Y.
87 Yamaguchi, The Brain/MINDS 3D digital marmoset brain atlas. *Sci Data*. **5**, 180009 (2018).
- 88 67. J. A. Bourne, M. G. P. Rosa, Preparation for the in vivo recording of neuronal responses in the
89 visual cortex of anaesthetised marmosets (*Callithrix jacchus*). *Brain Research Protocols*. **11**,
90 168–177 (2003).

- 91 68. K. A. Fritsches, M. G. P. Rosa, Visuotopic organisation of striate cortex in the marmoset
92 monkey (*Callithrix jacchus*). *J Comp Neurology*. **372**, 264–282 (1996).
- 93 69. H.-H. Yu, R. Verma, Y. Yang, H. A. Tibballs, L. L. Lui, D. H. Reser, M. G. P. Rosa, Spatial
94 and temporal frequency tuning in striate cortex: functional uniformity and specializations related
95 to receptive field eccentricity. *Eur J Neurosci*. **31**, 1043–1062 (2010).
- 96 70. F. Gallyas, Silver Staining of Myelin by Means of Physical Development. *Neurol Res*. **1**, 203–
97 209 (1979).
- 98 71. J. Schindelin, I. Arganda-Carreras, E. Frise, V. Kaynig, M. Longair, T. Pietzsch, S. Preibisch,
99 C. Rueden, S. Saalfeld, B. Schmid, J.-Y. Tinevez, D. J. White, V. Hartenstein, K. Eliceiri, P.
00 Tomancak, A. Cardona, Fiji: an open-source platform for biological-image analysis. *Nat Methods*.
01 **9**, 676–682 (2012).

02

03

04 **Acknowledgments**

05 The authors would like to acknowledge and thank D.A. Leopold who read through earlier
06 versions of the manuscript and M.J. de Souza for technical assistance and Qi Zhu Wu for MRI
07 acquisition and DTI preprocessing.

08

09 **Funding:**

10 This work was supported by National Health and Medical Research Council (NHMRC) Project
11 Grant APP1042893. W.C.K is supported by NHMRC Dora Lush Postgraduate Scholarship
12 APP1190007. J.A.B is supported by NHMRC Senior Research Fellowship APP1077677. The
13 Australian Regenerative Medicine Institute is supported by grants from the State Government of
14 Victoria and the Australian Government.

15

16 **Author Contributions:**

17 W.C.K. and J.A.B. conceived and designed the research. W.C.K., C-K.C., H-H.Y., I-C.M. and
18 J.A.B. designed the experiments. W.C.K., I-C.M., D.M.F, J.A.B. performed the MT ablation
19 surgeries. C-K.C., W.C.K., and D.M.F performed the behavioural experiments. C-K.C and D.M.F
20 analyzed the behavioural data. W.C.K., I-C.M., H-H.Y., J-H.L., J.A.B performed the
21 electrophysiology experiments. I-C.M. analyzed the MRI data. W.C.K performed all tissue
22 processing, immunolabelling and cell counts. W.C.K., C-K.C., H-H.Y. and J.A.B. wrote the
23 paper.

24

25 **Competing interests:** The authors declare that they have no competing interests

26

27 **Data and materials availability:** All data that supports the findings of this study are available
28 from the authors on reasonable request. See author contributions for specific datasets.