

Glutamatergic facilitation of neural responses in MT enhances motion perception in humans

Michael-Paul Schallmo^{1*}, Rachel Millin¹, Alex M. Kale¹, Tamar Kolodny¹, Richard A.E. Edden², Raphael A. Bernier³,
& Scott O. Murray¹

¹Department of Psychology, University of Washington, Seattle, WA

²Department of Radiology and Radiological Science, Johns Hopkins University, Baltimore, MD

³Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA

*corresponding author: schal110@umn.edu

F212/2C West Building

2450 Riverside Ave S

Minneapolis, MN 55454

Abstract

There is large individual variability in human neural responses and perceptual abilities. The factors that give rise to these individual differences, however, remain largely unknown. To examine these factors, we separately measured fMRI responses to moving gratings in the motion-selective region MT, and perceptual duration thresholds for motion direction discrimination within the same group of male and female subjects. Further, we acquired MR spectroscopy data that allowed us to quantify an index of neurotransmitter levels in the region surrounding MT. We show that individual differences in the Glx (glutamate + glutamine) signal in the MT region are associated with both higher fMRI responses and improved psychophysical task performance. Our results suggest that individual differences in baseline levels of glutamate within MT contribute to motion perception by increasing neural responses in this region.

Significance

What factors govern the relationship between neural activity and behavior? Our results suggest that one such factor is the level of glutamate, an excitatory neurotransmitter, within a particular region of cortex. By measuring an index of glutamate *in vivo* using magnetic resonance spectroscopy, we show that human subjects with more glutamate in the visual motion area known as MT also have larger fMRI responses (an index of neural activity) in this region. Further, people with more glutamate in MT can accurately perceive moving images presented more briefly within a behavioral task. Our findings point to an important role for glutamate levels in determining the relationship between neural responses and behavior during visual motion perception.

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48 Introduction

49 A direct relationship between greater neural responses and better perceptual functioning is well established in both
50 humans (Boynton et al., 1999) and animal models (Newsome et al., 1989; Britten et al., 1992). One factor that may
51 determine neural responsiveness and subsequent behavior is the amount of the neurotransmitter glutamate (Glu)
52 available within a given region of cortex. Glu is the primary excitatory neurotransmitter in cortex and is released from
53 presynaptic vesicles as the result of an action potential (Magistretti et al., 1999). Individuals with higher baseline Glu levels
54 in a particular region may therefore possess greater potential for excitation within the local neural population (Conti and
55 Weinberg, 1999). An index of Glu concentration can be measured non-invasively *in vivo* using MR spectroscopy (MRS).
56 Although MEGA-PRESS sequences (Mescher et al., 1998) are most often used to measure γ -aminobutyric acid (GABA)
57 levels, the difference spectrum that is obtained also contains a peak at 3.75 ppm associated with Glu. The size of this peak
58 is believed to reflect the level of Glu within the MRS voxel, which is considered a stable individual trait. However, both
59 Glutamine and Glutathione also contribute to the size of this peak (Mullins et al., 2014; Harris et al., 2017) – hence the
60 peak is often referred to as Glx, to signify that it is a combined measure of multiple metabolites (glutamate, glutamine, &
61 glutathione). Currently, it is not clear how Glx levels measured with MRS are related to the neural responses that support
62 behavior.

63 We hypothesized that greater regional concentrations of Glx would be associated with higher neural activity (reflected
64 in stronger fMRI responses) and in turn, superior performance on a task that depends on neural response magnitude. Our
65 group recently examined the role of GABA during motion perception in humans using MRS (Schallmo et al., 2018). Here,
66 we again chose to focus on neural processing within cortical area MT, in order to test our above hypothesis regarding a
67 link between Glx, neural responses, and task performance. Neural responses in MT in both monkeys (Britten et al., 1992;
68 Huk and Shadlen, 2005; Churan et al., 2008; Liu et al., 2016) and humans (Tootell et al., 1995; Rees et al., 2000; Tadin et
69 al., 2011; Turkozer et al., 2016; Chen et al., 2017; Schallmo et al., 2018) are known to be tightly linked to motion
70 perception. In particular, studies in humans suggest that motion duration thresholds (Tadin et al., 2003; Tadin, 2015) –
71 the amount of time that a stimulus needs to be presented to accurately discriminate motion direction – are shorter under
72 conditions that elicit higher MT responses (Tadin et al., 2011; Turkozer et al., 2016; Schallmo et al., 2018). Consistent with
73 our hypothesis, we observed a link between individual differences in Glx levels and fMRI response magnitudes within
74 human MT complex (hMT+): individuals with higher Glx had higher fMRI responses. Further, we found that both higher
75 Glx and larger fMRI responses were associated with reduced motion duration thresholds (superior performance). Overall,
76 our findings suggest that individual differences in the amount of Glu, as measured by MRS, contribute to motion direction
77 discrimination by facilitating neural responses within hMT+.

78 Methods

79 *Participants*

80 Twenty-two young adults participated (mean age = 24 years, $SD = 3.7$; 13 females and 9 males). These subjects were
81 included in two recent studies from our group examining the role of GABA in motion perception (Schallmo et al., 2018),
82 and sex differences in motion processing (Murray et al., submitted). Subjects were screened for having normal or
83 corrected-to-normal vision, no neurological impairments, and no recent psychotropic medication use. Further screening
84 prior to MRS scanning included: no more than 1 cigarette per day in the past 3 months, no recreational drug use in the
85 past month, no alcohol use within 3 days prior to scanning. Subjects provided written informed consent prior to
86 participation and were compensated \$20 per hour. All procedures were approved by the Institutional Review Board at the
87 University of Washington (approval numbers 48946 & 00000556) and conformed to the guidelines for research on human
88 subjects from the Declaration of Helsinki.

89 *Visual display and stimuli*

90 For fMRI, stimuli were presented using either an Epson Powerlite 7250 or an Eiki LCXL100A (following a hardware
91 failure), both with 60 Hz refresh rate. Images were presented on a screen at the back of the scanner bore and viewed
92 through a mirror mounted on the head coil. Images were shown using Presentation software (Neurobehavioral Systems,
93 Berkeley, CA). For psychophysics, a ViewSonic PF790 CRT monitor (120 Hz) was used with an associated Bits# stimulus
94 processor (Cambridge Research Systems, Kent, UK). Stimuli were presented on Windows PCs in MATLAB (MathWorks,

95 Natick, MA) using Psychtoolbox-3 (Brainard, 1997; Pelli, 1997; Kleiner et al., 2007). Viewing distance for both displays was
96 66 cm, and display luminance was linearized.

97 The visual stimuli were identical to those described previously (Schallmo et al., 2018). Briefly, drifting sinusoidal
98 luminance modulation gratings were presented with Gaussian blurred edges on a mean gray background. Grating contrast
99 was either 3% or 98%. Gratings were 2° in diameter for fMRI, and 0.84° in diameter for psychophysics. Spatial frequency
100 was 1 cycle/° (fMRI) or 1.2 cycles/° (psychophysics). Drift rate was 4 cycles/s for both experiments.

101 *Experimental procedure and data analysis*

102 Functional MRI

103 The fMRI paradigm has been described previously (Schallmo et al., 2018). Structural (1 mm resolution) and functional
104 data (3 mm resolution, 30 oblique-axial slices, 0.5 mm gap, 2 s TR) were acquired on a Philips 3T scanner. Before the fMRI
105 task scans, a 1-TR scan was acquired with the opposite phase-encode direction, which was used for distortion
106 compensation.

107 The fMRI task measured the response to drifting gratings presented at different contrast levels within a blocked
108 experimental design (Figure 1A). Sixteen gratings were presented within each block (400 ms duration, 225 ms inter-
109 stimulus interval, 10 s total block duration), which drifted in 8 possible directions (randomized & counterbalanced).
110 Stimulus contrast varied across block; this began with a 0% contrast (blank) block. Then, blocks of high (98%) and low
111 contrast (3%) gratings were presented in alternating order, each followed by a blank block to allow the fMRI response to
112 return to baseline (6 high, 6 low, and 13 blank blocks total). Task scans were 4.2 minutes long (125 TRs), and each subject
113 completed a total of 2-4 scans across 1 or 2 scanning sessions, as part of a larger set of visual fMRI experiments.

114 A functional localizer scan was also included in each scanning session, in order to identify regions-of-interest (ROIs).
115 This localizer was designed to identify human MT complex (hMT+); we did not attempt to distinguish areas MT and MST
116 (Huk et al., 2002). Drifting gratings (as above, but 15% contrast) alternated with static gratings across blocks (10 s block
117 duration, 125 TRs total). Bilateral hMT+ ROIs (averaged across subjects, in Talairach space) are shown in Figure 1C (yellow).

118 Subjects performed a fixation task during all fMRI scans. This involved responding to a green circle within a series of
119 colored shapes presented briefly at fixation (Figure 1A). This task encouraged subjects to focus their spatial attention at
120 the center of the screen and minimized eye movements away from this position.

121 fMRI data were analyzed using BrainVoyager (Brain Innovation, Maastricht, The Netherlands), and MATLAB (The
122 Mathworks, Natick, MA). Preprocessing was performed in the following order: motion correction, distortion
123 compensation, high-pass filtering (2 cycles/scan), co-registration, and transformation into the space of the individual
124 subject's T₁ anatomical scan. Normalization and spatial smoothing were not performed; all analyses were conducted
125 within ROIs for each individual subject. ROIs were defined using correlational analyses, as previously described (Schallmo
126 et al., 2018). ROI position was verified on an inflated model of the white matter surface. Analyses of fMRI time course data
127 was performed in MATLAB using BVQXTools. Data were broken into epochs spanning 4 s before the onset of each block
128 to 2 s after the offset. Average baseline responses were calculated across blocks separately for each condition (3% & 98%
129 contrast); this was computed as the average response to the blank background 0-4 s prior to block onset. Data were
130 converted to percent signal change, averaged across blocks, across ROIs from each hemisphere, and then averaged across
131 scanning sessions. Responses for each condition were defined as the mean of the fMRI signal peak (from 8-12 s following
132 block onset). For the correlational analyses (i.e., Figure 2C), fMRI responses to low and high contrast stimuli were
133 averaged, as an index of overall responsiveness.

134 Behavioral psychophysics

135 Subjects performed a psychophysical motion direction discrimination task outside of the scanner, during a separate
136 experimental session. This paradigm followed established methods (Tadin et al., 2003; Foss-Feig et al., 2013) and is
137 described in a recent paper from our group (Schallmo et al., 2018). In the full experiment, drifting gratings were presented
138 at 2 contrast levels (3% & 98%) and 3 sizes (0.84, 1.7, & 10° diameter). In order to minimize the effects of spatial
139 suppression / summation seen with larger stimuli (Tadin et al., 2003; Foss-Feig et al., 2013; Tadin, 2015; Schallmo et al.,
140 2018), only data from the smallest stimulus size were included in the current study. Thus, we focused on the smallest size
141 condition, wherein motion discrimination performance is expected to depend primarily on the magnitude of neural
142 responses driven by stimuli within the classical receptive field (Tadin, 2015).

143 In this task, subjects were asked to report
144 whether a briefly presented grating drifted
145 left or right (Figure 1B). The stimulus duration
146 was adjusted across trials (range 6.7 – 333
147 ms) using the Psi adaptive staircase method
148 within the Palamedes toolbox (Prins and
149 Kingdom, 2009; Kingdom and Prins, 2010), in
150 order to find the duration for which motion
151 discrimination performance reached 80%
152 accuracy. Trials began with a brief central
153 fixation mark (a shrinking circle; 850 ms),
154 followed by the presentation of the grating.
155 A fixation mark presented after the grating
156 cued the subjects to respond; response time
157 was not limited. Staircases were comprised
158 of 30 trials for each stimulus condition (3% &
159 98% contrast), presented in a randomized
160 counterbalanced order within each run. Run
161 duration was approximately 6 min. Subjects
162 completed 4 runs each, for a total experiment
163 duration of about 30 min, including
164 instructions and practice prior to the start of
165 the main experiment.

166 Data from each staircase were fit with
167 separate Weibull functions using the
168 Palamedes toolbox (Prins and Kingdom,
169 2009). Motion duration thresholds were
170 defined at 80% accuracy based on this fit.
171 When averaging across thresholds from
172 different conditions (i.e., for the correlations
173 in Figure 2D), the mean threshold was first
174 taken across runs in each condition, and then
175 the geometric mean was taken across
176 conditions, to account for the fact that
177 threshold ranges varied across conditions.

178 MR spectroscopy

179 Our MRS data acquisition was the same
180 as described previously (Schallmo et al.,
181 2018). Briefly, we used a MEGA-PRESS
182 (Mescher et al., 1998) sequence on a Philips
183 3T scanner. Sequence parameters were as
184 follows: 3 cm isotropic voxel, 320 averages,
185 2048 data points, 2 kHz spectral width, 1.4
186 kHz bandwidth refocusing pulse, VAPOR
187 water suppression, 2 s TR, 68 ms TE, 14 ms
188 editing pulses at 1.9 ppm for “on” and 7.5 ppm for “off” acquisitions, “on” and “off” interleaved every 2 TRs with a 16-
189 step phase cycle. Across 2 additional scanning sessions (separate from fMRI), MRS data were acquired from the following
190 3 regions: 1) lateral occipital cortex, centered on hMT+ (Figure 1C); 2) mid-occipital region of early visual cortex (EVC),
191 parallel to the cerebellar tentorium; 3) fronto-parietal cortex (FPC), centered on the “hand-knob” (Yousry et al., 1997) .

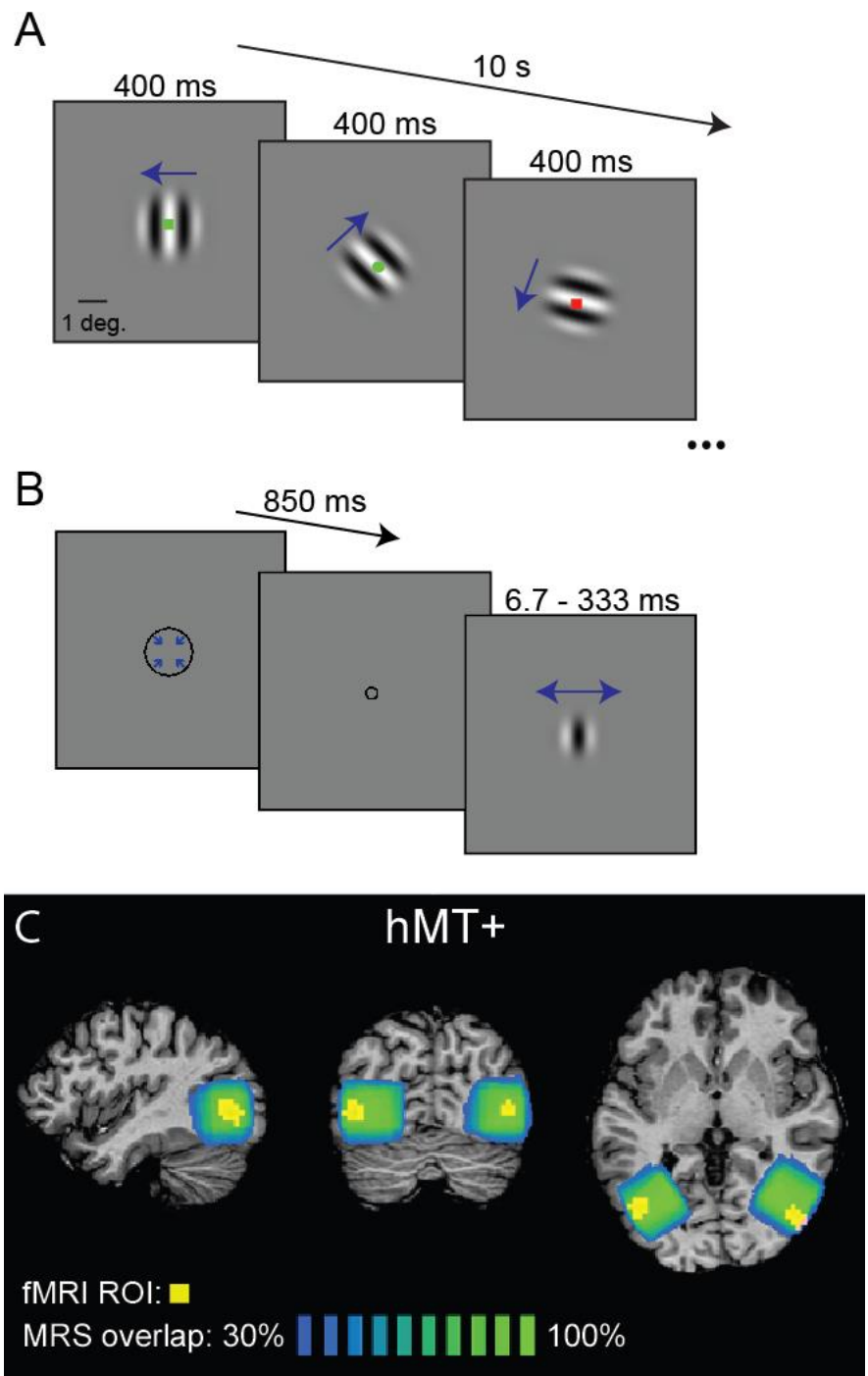


Figure 1. Visual stimuli and MR spectroscopy. **A** shows the fMRI task timing (10 s blocks of 400 ms drifting gratings). Blue arrows indicate motion direction. Fixation task stimuli also shown. **B** shows the timing of a psychophysics trial from the task performed outside the scanner (850 ms cue, variable grating duration). Average MRS voxel placement is shown in **C** (adapted from Schallmo et al., 2018). Green-blue color indicates the percent overlap of the fMRI-localized MRS voxels in the hMT+ region (in Talairach space) across all subjects. Average hMT+ ROIs from fMRI for all subjects are shown in yellow (threshold correlation between predicted & observed fMRI timeseries $r \geq 0.3$).

Voxels in hMT+ were positioned using an on-line functional localizer (moving vs. static, as above); left and right hMT+ was measured for each subject, typically within the same scanning session. For EVC and FPC, voxels were positioned based on each individual's anatomical landmarks; see (Schallmo et al., 2018) for images of these voxel positions. Data were acquired in EVC across 2 separate scans (typically in different sessions; 1 subject had only 1 EVC scan). Only 1 scan was acquired in FPC (1 subject did not complete the FPC scan). Subjects watched a film of their choice during MRS, with images presented on the screen (as above, for fMRI), and audio presented through MR-compatible headphones. MRS, fMRI, and psychophysical data were collected within a 2-week period for all subjects. Previous work suggests metabolite measurements from MRS are stable over the course of several days (Evans et al., 2010; Greenhouse et al., 2016).

MRS data were analyzed using the Gannet toolbox version 2.0 (Edden et al., 2014). Automated processing steps within this toolbox were as follows: frequency and phase correction, artifact rejection (frequency correction > 3 SD above the mean), and exponential line broadening (3 Hz). The Glx peak at 3.75 ppm was fit with a double-Gaussian function (Figure 2A & B); the integral of this function served as the measure of Glx concentration. Note that this fitting was performed separately from fitting the GABA peak at 3 ppm. The value of Glx was scaled by the integral of the water peak for each individual. Correction for gray / white matter content within the voxel was not performed.

No significant correlations were observed between the concentration of unsuppressed water (fit by Gannet) in hMT+ and either fMRI response magnitudes ($r_{20} = -0.37$, FDR corrected 2-tailed $p = 0.081$) or psychophysical thresholds ($r_{20} = 0.44$, FDR corrected 2-tailed $p = 0.080$). However, as these correlations were moderately strong (despite not reaching statistical significance), the effect of scaling Glx values to water merits further consideration. Since we observed qualitatively similar results to those presented below when scaling Glx to creatine instead of water (not shown), we believe it is reasonable to conclude that the observed correlations are driven by a genuine relationship between Glx, fMRI, and motion thresholds, rather than being attributable to water scaling.

Statistics

Statistical analyses were performed in MATLAB. Because variance differed for duration thresholds at low and high contrast, Friedman's non-parametric ANOVA was used for this comparison. One tailed Pearson's correlation coefficients were calculated for all correlational analyses; this is justified by the strong *a priori* hypotheses being tested and is noted for each occurrence in the Results. Correlation significance was further examined using (non-parametric) permutation tests, which involved randomly shuffling the data being correlated across subjects in each of 10,000 iterations. The proportion of permuted correlations with coefficients greater (or more negative) than that of the observed, un-shuffled correlation served as the measure of significance (the p -value).

Results

Using MR spectroscopy, we measured the concentration of glutamate (plus co-edited metabolites; Glx; Figure 2A & B) within the motion selective region of human MT complex (hMT+). We sought to determine whether individual differences in Glx concentration were positively associated with neural responsiveness during motion perception, as indexed with fMRI. fMRI signals were measured in hMT+ in response to moving gratings with low (3%) and high (98%) luminance contrast (Figure 2C). Responses were larger for high than for low contrast stimuli (1-tailed paired $t_{21} = 8.02$, $p = 4 \times 10^{-8}$), as expected (Tootell et al., 1995). An overall index of fMRI responsiveness was obtained for each subject by averaging the peak response to both low and high contrast (gray regions; Figure 2C). As predicted, there was a significant positive correlation between average fMRI responses in hMT+ and concentrations of Glx in the same region (Figure 2D; $r_{20} = 0.54$, 1-tailed $p = 0.022$; FDR corrected). These results suggest that individuals with more Glx in the region surrounding area MT have larger neural responses to moving stimuli, consistent with stronger glutamatergic excitation.

We next examined whether individual differences in Glx concentration in the region surrounding hMT+ were associated with behavioral differences in motion discrimination. We measured motion duration thresholds (Tadin et al., 2003; Tadin, 2015) to small (0.84°) gratings of low and high contrast (Figure 2E). Duration thresholds were smaller for high vs. low contrast stimuli (Friedman's $\chi^2_1 = 30$, $p = 4 \times 10^{-8}$), consistent with previous findings (Tadin et al., 2003; Foss-Feig et al., 2013). To obtain an overall measure of motion perception, duration thresholds were averaged across low and high contrast. We observed the predicted relationship between Glx in hMT+ and average motion duration thresholds; individuals with greater Glx showed lower thresholds (superior performance; Figure 2F; $r_{20} = -0.44$, 1-tailed $p = 0.042$; FDR

239 corrected). The relationship between
240 duration thresholds and Glx was specific to
241 hMT+; we saw no significant correlations
242 between thresholds and Glx in two other
243 MRS voxels (early visual cortex [EVC] and
244 fronto-parietal cortex; $|r_{20}| < 0.23$,
245 uncorrected p -values > 0.14).

246 The significant positive correlation
247 between Glx and fMRI response magnitudes,
248 and the negative correlation between Glx and
249 duration thresholds together suggest a
250 negative relationship may exist between
251 fMRI responses and duration thresholds.
252 Indeed, we observed a significant negative
253 correlation ($r_{20} = -0.60$, 1-tailed $p = 5 \times 10^{-4}$);
254 higher averaged fMRI responses in hMT+
255 were associated with lower averaged
256 duration thresholds, consistent with our
257 observations from a separate analysis of
258 different stimulus conditions within the same
259 dataset (Murray et al., submitted). Taken
260 together, our findings are consistent with the
261 idea that stronger glutamatergic excitation
262 drives larger neural responses in hMT+ during
263 motion perception, thereby facilitating lower
264 duration thresholds (i.e., superior motion
265 discrimination).

266 The concentration of Glx showed some
267 specificity between regions. Glx
268 concentrations in hMT+ showed some
269 association with Glx in EVC, but this did not
270 survive correction for multiple comparisons
271 ($r_{20} = 0.43$, 1-tailed $p = 0.023$, uncorrected; $p =$
272 0.069 after FDR correction). Neither hMT+ nor
273 EVC concentrations were significantly
274 associated with Glx in fronto-parietal cortex
275 ($|r_{20}| < 0.37$, FDR corrected 1-tailed p -values
276 > 0.097).

277 Recent work from our group has demonstrated a small but statistically reliable gender difference in motion
278 discrimination thresholds, with females showing slightly higher duration thresholds on average than males (Murray et al.,
279 submitted). Thus, we examined whether there might be gender differences in Glx levels in hMT+ as well. However, no
280 significant difference in hMT+ Glx was observed between males (mean = 1.33 i.u., $SD = 0.10$) and females (mean = 1.34 i.u.,
281 $SD = 0.10$; 2-tailed independent samples $t_{20} = 0.17$, $p = 0.87$). This is concordant with our recent finding (Murray et al.,
282 submitted) that fMRI response magnitudes in hMT+ also did not differ between genders (despite the significant difference
283 in psychophysical thresholds for the same subjects). The lack of a gender difference in Glx may reflect the fact that,
284 although neural processing in MT clearly influences motion perception, response magnitudes in MT are not the only factor
285 that determine duration thresholds for motion discrimination.

286 We also examined whether the observed relationships between Glx and fMRI or motion discrimination thresholds
287 might in fact be attributable to GABA levels, possibly as an artifact of the MRS sequence. Although a Glx peak is obtained

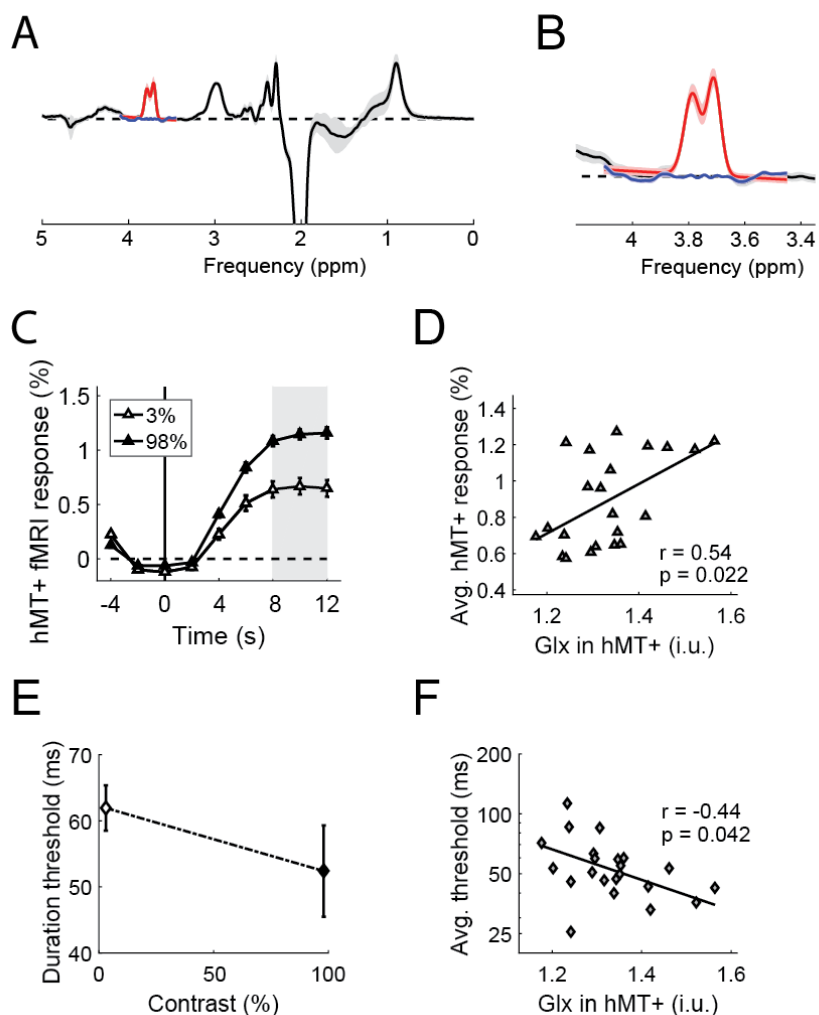


Figure 2. A link between Glx, fMRI, and motion duration thresholds. **A** shows the MR spectra (black), fits to the Glx peak (red) and residuals (blue) averaged across subjects. Error bars in **A** & **B** show SD . **B** shows a zoomed-in view of the data from **A**. Panel **C** shows the time course of fMRI responses measured in hMT+, averaged across subjects. Peak response was calculated within the gray region. Higher Glx in hMT+ correlates significantly with greater fMRI responses in the same area (**D**; averaged across contrasts). Duration thresholds are shown in **E**; these correlated negatively with Glx in hMT+ (**F**; geometric mean of thresholds across contrasts). Error bars in **C** & **E** show SEM .

288 using MEGA-PRESS, this sequence is typically used to measure the concentration of an edited GABA peak at 3 ppm, which
289 is acquired in the same scan (Mescher et al., 1998; Mullins et al., 2014). We have previously observed that higher GABA
290 concentrations in hMT+ correlate with lower motion discrimination thresholds within the same group of subjects
291 (Schallmo et al., 2018). Thus, we sought to determine whether the current relationships with Glx might be accounted for
292 by the previously reported relationship with GABA – perhaps due to homeostatic processes balancing the levels of these
293 neurotransmitters, the manner in which they were measured together using MEGA-PRESS, and/or the method of
294 quantifying both peaks in Gannet (Edden et al., 2014). However, we observed no significant correlations between Glx and
295 GABA measurements across individuals in any of the 3 ROIs that we examined (not shown; all $|r_{(20)}| < 0.34$, 2-tailed p -
296 values > 0.14 ; uncorrected), suggesting that the Glx results presented here cannot be explained by the amount of co-
297 measured GABA.

298 Discussion

299 To our knowledge, this is the first study to present evidence of a 3-way link between behavioral performance, BOLD
300 response magnitudes, and Glx levels in humans. These findings help to clarify the role of glutamate in visual motion
301 perception, and suggest that higher excitatory tone (as measured by Glx from MRS) facilitates larger neural responses and
302 greater perceptual sensitivity. A straightforward association between higher levels of Glx, larger fMRI responses, and
303 superior performance is perhaps not surprising. However, our findings are notable, given that the relationships between
304 each of these measures and the underlying neural responses are complex (Logothetis, 2008; Duncan et al., 2014; Harris
305 et al., 2015). Adding to this complexity, Glu also plays an important role in cell metabolism (Magistretti et al., 1999) in
306 addition to functioning as a neurotransmitter.

307 It is still unclear how measures of Glx from MRS are tied to changes in neural activity in the human brain (Duncan et
308 al., 2014). Studies using functional MRS at 7 Tesla to measure Glu show increased occipital Glu following visual stimulation,
309 and support the idea that the magnitude of Glu being measured depends on the level of local neural activity (Mangia et
310 al., 2007; Lin et al., 2012; Schaller et al., 2013; Apšvalka et al., 2015). However, it is not yet known to what extent the Glu
311 being measured with MRS reflects a ‘direct’ relationship with neural activity (i.e., driven by Glu neurotransmission) vs. an
312 ‘indirect’ one (i.e., reflects Glu’s role in cell metabolism, which is affected by spike rate). It has been argued that Glu
313 becomes more MR visible as it moves from pre-synaptic vesicles to the synaptic cleft during neurotransmission and into
314 astrocytes following reuptake, and that this change in MR visibility may suggest that Glx measured with MRS reflects Glu
315 release during neurotransmission (Apšvalka et al., 2015). Alternatively, higher rates of neural activity might also increase
316 the rate of Glu cycling through the synaptic cleft, which could lead to a transient buildup of Glu (depending on the rate
317 limiting step in this cycle; Lin et al., 2012). While the 3-way association between Glx, fMRI, and behavior in the current
318 study is consistent with the idea that Glx levels reflect the strength of glutamatergic neurotransmission, direct
319 experimental support for this hypothesis remains lacking.

320 Our work helps to clarify how glutamate in human visual cortex supports visual behavior. We are aware of very few
321 studies examining how visual perception is related to individual differences in Glx measurements. Some have found that
322 higher occipital Glx measurements are associated with increased visual functioning (Terhune et al., 2015; Wijtenburg et
323 al., 2017), while others have not (Pugh et al., 2014; Takeuchi et al., 2017). One study from the latter category found that
324 frontal Glx levels, but not measurements in MT, were associated with individual differences in an ambiguous motion
325 perception task (Takeuchi et al., 2017). The discrepancy with the current findings may be explained by the manner in
326 which visual behavior was assessed (i.e., ambiguous motion vs. direction discrimination). The association between lower
327 motion duration thresholds (better performance) and greater Glx in MT from the current study suggests that motion
328 discrimination performance is facilitated by higher levels of Glu, likely due to greater excitatory neural activity within area
329 MT.

330 The role of area MT in visual motion perception is well established (Born and Bradley, 2005; Zeki, 2015), but the
331 manner in which individual differences in MT responsiveness relate to differences in perception is less clear. In a seminal
332 study, Rees and colleagues (Rees et al., 2000) demonstrated a positive linear relationship between the coherence of
333 moving dot stimuli and the fMRI response in human MT. They also reported modest individual variability in the coherence-
334 response function, but not whether such variability corresponds to differences in perception. A more recent study has
335 found a correspondence between improved behavioral performance and fMRI response changes in MT following

336 perceptual learning (Chen et al., 2017). Specifically, subjects with smaller thresholds in a motion discrimination paradigm
337 following extensive training also showed greater sharpening of tuning within MT, as assessed by multi-voxel pattern
338 analysis. This suggests that increased selectivity within MT is important for learning to perform a motion discrimination
339 task.

340 Here, we used a variation of a well-established motion discrimination paradigm (Tadin et al., 2003; Foss-Feig et al.,
341 2013; Tadin, 2015), in which larger neural responses (particularly within area MT) are thought to facilitate motion direction
342 discrimination for more-briefly presented stimuli, resulting in shorter duration thresholds (i.e., better performance).
343 Evidence for the role of neural activity in MT within this paradigm has been provided by studies in both macaques (Liu et
344 al., 2016) and humans (Tadin et al., 2011; Turkozer et al., 2016; Schallmo et al., 2018). Our current findings build upon this
345 work and suggest that individual differences in Glu concentration in area MT contribute to the neural responsiveness
346 within the region, as well as consequent motion discrimination performance. Measuring Glu may thus provide valuable
347 insight into the neural basis of individual differences in visual perception.

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