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2 **An inability to exclude visual noise in migraine.**

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Running title: Visual noise in migraine.

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1. Abstract:

Purpose: People with migraine are relatively poor at judging the direction of motion of coherently-moving signal-dots when interspersed with noise-dots drifting in random directions, a task known as motion coherence. Although this has been taken as evidence of impoverished *global* pooling of motion signals, it could also arise from unreliable coding of *local* direction (of each dot), or an inability to segment signal from noise (*noise-exclusion*). The aim of this study was to determine how these putative limits contribute to impoverished motion processing in migraine.

Methods: Twenty-two participants with migraine (mean age: 34.7±8.3 years; 16 female) and 22 age and sex matched controls (mean age: 34.4±6.2 years) performed a motion coherence task and a motion equivalent noise task, the latter quantifying *local* and *global* limits on motion processing. In addition, participants were tested on analagous equivalent noise paradigms involving judgements of orientation and size, so that the specificity of any findings (to visual dimension) could be ascertained.

Results: Participants with migraine exhibited higher motion coherence thresholds than controls ($p=0.01$, independent t-test). However, this difference could not be attributed to deficits in either local or global processing since they performed normally on all equivalent noise tasks ($p>0.05$, multivariate analyses of variance).

Conclusions: These findings indicate that motion perception in the participants with migraine was limited by an inability to exclude visual noise. We suggest that this is a defining characteristic of visual dysfunction in migraine, a theory that has the potential to integrate a wide range of findings in the literature.

42 **2. Introduction:**

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44 Migraine is an episodic disorder characterised by throbbing (commonly unilateral)
45 head pain, which may be accompanied by nausea, vomiting and an aversion to sound
46 or light¹. In approximately 30% of cases, a transient sensory and/or motor disturbance
47 known as an aura is also experienced². Certain visual stimuli can also trigger a
48 migraine attack³ and numerous studies have shown that individuals with migraine
49 exhibit subtle differences in visual psychophysical performance, both ictally and
50 interictally (see reviews^{4,5}). This is particularly the case for tasks involving
51 judgements of visual motion⁶.

52

53 Processing of visual motion relies on at least two hierarchical processing stages. In the
54 primary visual cortex (area V1), motion is processed *locally*, i.e. cells are sensitive to
55 the direction of motion within a small region of space⁷. This information is then
56 relayed to the medial temporal (MT) and medial superior temporal (MST) areas,
57 where it is integrated to form a global motion percept⁸. People with migraine
58 seemingly process *local* motion normally, since they perform as well as a control
59 group when asked to discriminate or classify the direction of a stimulus containing a
60 single direction of motion^{6,9-11}. However, people with migraine perform relatively
61 poorly on motion coherence tasks where the participant must classify the direction of
62 motion of a set of signal-dots moving coherently (in one direction) but interspersed
63 with noise-dots drifting in random directions (Fig. 1A)^{6,9,10,12-14}.

64

65 Since the signal-direction in a coherence task cannot be determined from a single
66 dot's trajectory, the participant must make a judgement of *global* motion direction. As
67 a result, high motion coherence thresholds are often taken as evidence of a selective
68 deficit in global motion pooling. However, motion coherence judgements can be
69 limited not only by global integration, but also, by unreliable *local* processing¹⁵. This
70 could be the case, for example, if higher cortical areas inherit input from V1 cells
71 prone to high levels of random firing, i.e. elevated internal noise. A further limit on
72 motion coherence performance is defined by an observer's ability to segregate *signal*
73 from *noise* dot directions. Thus, computational models show that human observers
74 perform much better on coherence tasks than would be expected if they used a pure
75 pooling strategy^{15, 16}, suggesting that they are capable of selectively monitoring
76 directions of interest.

77

78 To try and disentangle these putative limits to motion processing we used a technique
79 known as equivalent noise (EN) analysis. This psychophysical paradigm allows
80 performance to be parcellated into *independent* estimates of local and global
81 processing¹⁷. Similar to the motion coherence paradigm, EN analysis requires
82 participants to classify the direction of motion of signal dots that are corrupted by
83 noise¹⁵. However, in EN analysis, noise is added by manipulating the standard
84 deviation of the distribution of directions presented, rather than adding noise dots that
85 drift in random directions (Fig. 1B). As a result, every dot contributes to the signal,
86 and the optimum strategy is to integrate *all* directions of motion in the stimulus.
87 Consequently, an estimate of global processing is obtained that does not rely on the
88 participants' ability to exclude noise. Further, by measuring performance in the

89 absence (as well as in the presence) of noise, an independent estimate of a
90 participant's ability to process information locally is also available.

91

92 We sought to determine if motion processing in migraine is (a) limited by local
93 processing, global processing and/or noise exclusion, and (b) part of a more general
94 integration deficit. To this end, participants with and without migraine were tested on
95 a series of matched psychophysical tasks. A motion coherence paradigm was used to
96 assess each participant's ability to classify the direction of signal motion whilst
97 excluding random noise. Independent estimates of local and global motion processing
98 performance were obtained using a motion EN paradigm. Finally, to assess the
99 specificity of any findings to motion processing participants undertook analagous EN
100 tasks that probed local and global processing for judgements of orientation and size.

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102 **3. Materials and Methods:**

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104 Ethics approval was granted by the University of East London Psychology Research
105 Ethics Committee and the Department of Psychological Sciences Ethics Committee at
106 Birkbeck College. Informed written consent was obtained from each participant in
107 accordance with the declaration of Helsinki.

108

109 **Participants**

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111 Data were gathered from 22 participants with migraine (MG) and 22 migraine-free
112 control participants (CON) (Table 1). The two groups were matched for sex (16

113 female) and did not differ significantly with respect to age [mean age: 34.7±8.3 (MG)
114 and 34.4±6.2 years (CON); $t_{(42)}=0.04, p=0.97$]. All participants with migraine fulfilled
115 the International Headache Society (2004) diagnostic criteria for migraine without
116 aura (MO) or migraine with visual aura (VA), and had been diagnosed previously by a
117 general practitioner or neurologist. All participants had a minimum visual acuity of
118 20/20 binocularly (with or without optometric correction). No participant had a
119 history of mental illness and none were taking daily medication at the time of testing.

120

121 **General procedure**

122

123 The experiment lasted 60-75 minutes and consisted of: (i) a brief test of visual acuity
124 (assessed using a hand-held LogMar near visual acuity chart); (ii) a customised
125 questionnaire about basic demographics and migraine history; (iii) a motion
126 coherence paradigm; (iv) three EN paradigms, which probed local and global
127 processing for judgements of visual orientation, motion and size (separately).
128 Individual EN and coherence tasks were blocked and presented in a random order to
129 avoid sequence effects. All responses were given verbally and relayed to the computer
130 by the experimenter.

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132 **Motion Coherence procedure**

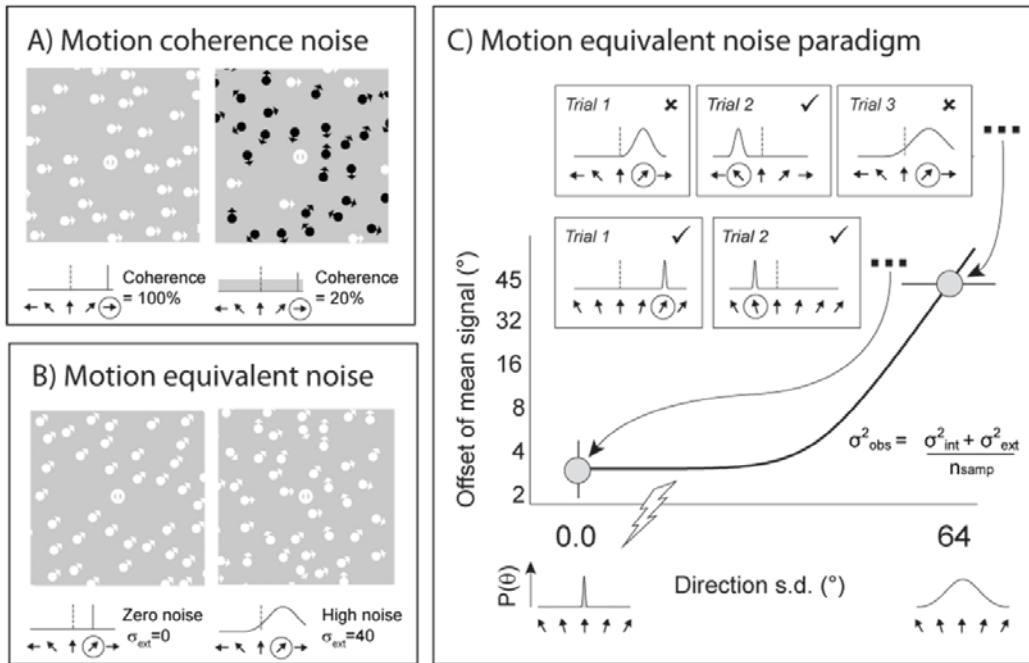
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134 Participants classified the direction of motion of a number of coherently moving dots
135 (the signal) embedded in noise. All signal dots were restricted to motion in the
136 horizontal plane (all left or all right on any given trial). Noise was added to the

137 stimulus by assigning a subset of dots directions of motion that were randomly
138 sampled from a flat distribution (Fig. 1A). Under the control of QUEST¹⁸, an adaptive
139 staircase procedure manipulated the level of coherence on each trial, where coherence
140 was defined as the percentage of dots that constituted the signal. The staircase
141 converged on the level of coherence necessary for each participant to correctly
142 ascertain the direction of motion on 82% of trials: the motion coherence threshold (see
143 Supplementary Fig. 1A for further details). Lower coherence thresholds therefore
144 reflected superior performance, indicating that the participant needed fewer signal
145 dots to correctly identify the direction of signal motion. The staircase terminated after
146 75 trials and was preceded by 15 practice trials.

147 **Table 1. Migraine group demographics and details of migraine history.** Details are provided for:
 148 (1) Type (MO: migraine without aura; VA: migraine with visual aura); (2) Sex (F: female; M: male);
 149 (3) Age; (4) Onset (age of migraine onset); (5) Freq 1 (number of migraine attacks experienced within
 150 the last three months); (6) Freq 2 (number of migraine attacks experienced within the last year); (7)
 151 Last (time, in weeks, since last migraine attack); (8) Duration (average duration, in hours, of a migraine
 152 attack when painkillers are administered); (9) Severity (index of migraine severity, derived from the
 153 multiplication of average migraine duration by the number of years migraine has been experienced).

Type	Sex	Age	Onset	Freq 1	Freq 2	Last	Duration	Severity
MO	F	21	13.5	1	3.5	8	60	144
MO	F	25	23	4	16	2	6.5	192
MO	F	38	16	4	20	1	24	384
MO	F	39	30	3.5	12	1	24	144
MO	F	40	5	6	24	2	48	517.5
MO	F	43	32	3	10	4	60	108
MO	M	23	16	2	6.5	4	24	32
MO	M	34	11.5	2	3	5	96	26.25
MO	M	38	28	3	10	3	4	22.5
MO	M	40	5.5	3	15	2.5	60	80
VA	F	21	10	3	12	2	6.5	100
VA	F	24	19	12	182	0.29	4.5	1536
VA	F	29	22	1	7.5	1.5	36	132
VA	F	30	14	3	12	3	6.5	440
VA	F	32	28	5	20	2	24	52.5
VA	F	33	10.5	0	1	30	24	840
VA	F	36	18	1.5	8	2	60	1575
VA	F	40	32	8	18	1	72	67.5
VA	F	44	28	5	24	1	10	45.5
VA	F	51	25	2	6.5	3	48	169
VA	M	38	6	12	48	0.29	12	110
VA	M	44	12.5	0	50	16	24	910
Mean		34.68	18.43	3.82	23.14	4.30	33.36	346.72
Stdev		8.25	8.81	3.26	37.65	6.66	25.89	463.62



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Figure 1. Psychophysical procedures. (A) Example high (100%) and low (20%) coherence motion stimuli. Signal dots are shown in white and noise dots in black. Directions of motion are indicated by the orientation of the arrow-heads. (Note: in the actual experiment all dots were white). Below each example stimulus is shown the corresponding distribution of signal values (solid black line) and noise values (dark grey shaded region). In the coherence task, noise was increased by changing the proportion of signal to noise dots. (B) Zero and high noise motion stimuli, with corresponding distributions of motion directions. In the equivalent noise task, noise was added by increasing the standard deviation of motion directions in the stimuli. In the plots of signal and noise distributions, the reference direction is denoted by a vertical black dotted line; the (average) direction of signal motion is circled. (C) The equivalent noise function (solid black line) is constrained by 2 data-points: the ‘zero noise’ threshold, which represents the minimum directional offset that can be reliably discriminated, and the ‘high noise’ threshold, which represents the maximum level of noise that can be tolerated for a large directional offset. The function has two parameters (inset in C), providing estimates of internal noise and global sampling (see Supplementary Material).

170 **Equivalent noise procedure**

171

172 A fast, efficient version of the EN paradigm, adapted for use with clinical populations,
173 was used to assess local and global processing limits. In the EN tasks, participants
174 judged whether a number of signal elements, presented for a brief duration were, on
175 average, drifting clockwise or anti-clockwise of vertical-upward motion (motion task;
176 Fig. 1B), tilted to the left or right of vertical (orientation task; Supplementary Fig.
177 2A), or smaller or larger than a reference (size task; Supplementary Fig. 2B). The
178 reference direction, orientation and size were defined by the fixation guide itself,
179 which was comprised of a small white circle bisected by a vertical line (identical in all
180 tasks).

181

182 Two independent staircases were randomly interleaved: a ‘zero noise’ and a ‘high
183 noise’ condition (Fig. 1C). In the zero noise condition, external noise was set to zero
184 and the staircase tracked the minimum orientation offset from vertical (orientation
185 task), directional offset from vertical (motion task) or size offset from reference (size
186 task) that could be reliably classified (Supplementary Fig. 1B). In the high noise
187 condition, the staircase tracked the maximum level of external noise that could be
188 tolerated for a large (fixed) signal offset (Supplementary Fig. 1C). In this condition,
189 the signal level was fixed at $\pm 22.5^\circ$ for the orientation, $\pm 45^\circ$ for the motion and ± 0.5
190 octaves for the size task. These values were selected on the basis of previous studies
191 and pilot data^{15, 19, 20}. Both staircases terminated after 75 trials each. As *per* the
192 coherence task, the staircases were under the control of QUEST and converged on
193 82% correct thresholds. For each participant and task a two-parameter EN function
194 was fit to their data, providing estimates of internal noise (a measure of local

195 processing) and sampling (global processing). (See Fig. 1C and Supplementary
196 Materials). To accustom participants to the nature of the task, all test blocks were
197 preceded by 15 practice trials. In addition, for a subset of observers (10 participants
198 with migraine and 8 without), 15 catch trials were randomly interleaved into each EN
199 paradigm. On each catch trial the stimulus was presented at a large signal level in the
200 absence of external noise ($\pm 22.5^\circ$, $\pm 45^\circ$ and ± 0.5 octaves for orientation, motion and
201 size tasks).

202

203 **Stimulus parameters**

204

205 All stimuli were generated in Matlab (MathWorks, Cambridge, MA) using the
206 Psychophysics Toolbox extensions^{21, 22} and were presented on a MacBook Pro laptop
207 computer that was connected to a luminance-calibrated LCD monitor at a spatial and
208 temporal resolution of 1920x1080 pixels and 60Hz, respectively.

209

210 Test images were generated by randomly dropping 100 elements (disks) within a
211 circular region with a diameter of 15° . For motion and size judgements, individual
212 elements could overlap. In the motion task, overlapping elements led to occlusion. In
213 the size task, the contrasts of overlapping elements were summed. For the orientation
214 task, element overlap was avoided by ensuring that adjacent elements were separated
215 by a minimum distance equal to twice their diameter. The resulting images were
216 presented in the centre of the screen for 400 milliseconds against a background grey
217 display. Stimuli were viewed in a dark room from a distance of 51 cm. The fixation
218 guide had a diameter of 0.44° .

219

220 For the orientation task, individual disks were comprised of random phase sine-wave
221 gratings with a spatial frequency of 3.4 cycles per degree presented at 50% contrast in
222 a circular hard-edged mask with a diameter of 0.44° (Supplementary Fig. 1A). For the
223 size task individual disks had the same characteristics as for orientation, but varied in
224 size and were randomly oriented (Supplementary Fig. 1B). The spatial frequency of
225 the grating was scaled to the diameter of the disk such that the number of cycles
226 presented remained constant across changes in size. In addition, for the size task, the
227 contrast of individual disks was randomly jittered in the range of 25-75% (sampled
228 from a flat distribution) in order to minimise the availability of contrast cues. For the
229 motion tasks, white dots with a diameter of 0.44° were used instead of windowed
230 gratings (Fig. 1B). Individual dots had a lifetime of 300ms, were spatially updated
231 every 50ms, moved at $3^\circ/\text{sec}$ and were presented at 50% contrast.

232

233 **Data transformation and filtration**

234

235 All variables, with the exception of age and age of migraine onset, were log
236 transformed as this typically reduced skew and kurtosis. Following this
237 transformation, the distribution of variables did not differ significantly from normal
238 ($p_s > 0.05$; one-sample Kolmogorov-Smirnoff tests). Data were then filtered
239 (separately for CON, MO and VA groups) so that extreme outliers with respect to
240 parameter estimates and associated confidence intervals (> 2.58 Z-scores from the
241 group mean) were excluded from analysis. This led to the exclusion of 5.42% of the
242 data, which represented outliers that were seemingly randomly distributed across the
243 different groups [migraine (1.75%); control (3.67%)], tasks [motion coherence

244 (0.87%); motion EN (1.05%); orientation EN (1.22%); size EN (2.27%)] and
245 individual participants.

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247 **4. Results**

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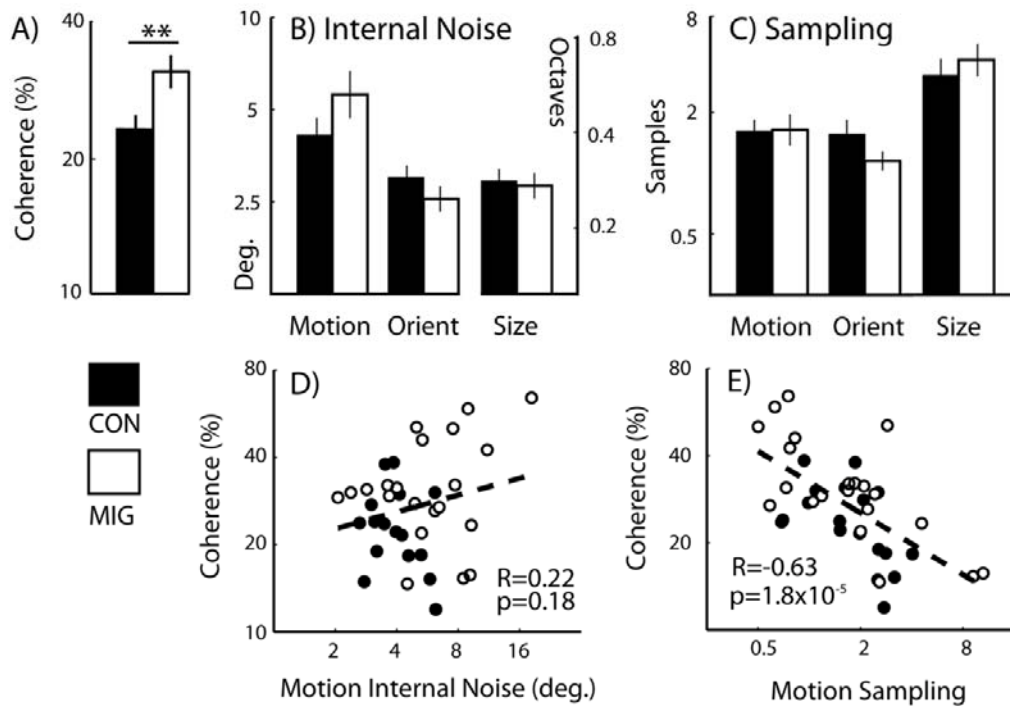
249 None of the variables of interest differed significantly between migraine sub-groups
250 (MO and VA) (independent t-tests, $ps>0.05$); consequently, MO and VA data were
251 pooled for all subsequent analyses. The percentage of catch trials answered correctly
252 was at ceiling, and did not differ between groups or across tasks (ANOVA, $ps>0.05$).

253

254 **Motion coherence thresholds**

255

256 To determine whether performance on the motion coherence task differed between
257 migraine and control groups (Fig. 2A), coherence thresholds were analysed using an
258 independent t-test (Table 2). A one-tailed test was employed since there are multiple
259 reports of elevated coherence thresholds in migraine (see Introduction). Motion
260 coherence thresholds were elevated in the migraine group ($32\pm 3.3\%$) relative to the
261 control group ($24\pm 1.8\%$) ($t_{(37)}=-2.37$, $p=0.01$, Cohen's $d=0.78$), requiring a higher
262 proportion of signal to noise dots to reliably classify the direction of signal motion.



264

265 **Figure 2. Coherence and equivalent noise plots.** Group mean (A) coherence thresholds, (B) levels of
 266 internal noise and (C) sampling are shown for control and migraine participants. Scatter-plots show
 267 correlations between motion coherence thresholds and (D) motion internal noise and (E) motion
 268 sampling. Error bars denote the standard error of the mean. Deg. = degrees. Note: data have been log-
 269 transformed; however, for ease of interpretation, axis tick-marks denote equivalent untransformed
 270 values.

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Table 2. Comparing group performance on motion coherence and equivalent noise tasks. Migraine and control group performance were compared using independent t-tests. Appropriate corrections were made to the degrees of freedom (d.f.) where equal variances could not be assumed. *P* values reported are for two-tailed tests, with the exception of the analysis of motion coherence thresholds, for which a single-tailed test was used (corrected alpha=0.1) (see text for further details). Bonferroni corrections were made for three multiple comparisons in the analysis of equivalent noise measures, reflecting the three different visual dimensions tested (corrected alpha=0.0167). *t*=t-statistic; d.f.=degrees of freedom; *p*=significance level; Cohen's *d*=effect size; *Th*=motion coherence threshold; σ_{int} =internal noise; n_{samp} =sampling. *significant effect at the stated alpha level.

		t	d.f.	<i>p</i>	Cohen's d
Coherence	Th	-2.37	37	*0.01	0.78
Motion	σ_{int}	-2.33	33.02	0.03	0.71
	n_{samp}	-0.04	41	0.97	0.02
Orientation	σ_{int}	1.21	41	0.23	0.38
	n_{samp}	1.82	32.56	0.08	0.59
Size	σ_{int}	0.22	39	0.83	0.07
	n_{samp}	-0.67	38	0.51	0.22

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Table 3. Predicting motion coherence thresholds. A regression analysis showing the prediction of motion coherence thresholds from variance in three predictor variables [motion internal noise, motion sampling and group (migraine or control)]. All variables were added to the model simultaneously (i.e. non-hierarchically). *Beta*=beta coefficient; *Beta_{st}*=standardized beta coefficient; *t*=t-statistic; *p*=significance level; σ_{int} =internal noise; n_{samp} =sampling. *predicts a significant proportion of unique variance in the outcome variable.

Predictor	Beta	Beta_{st}	t	<i>p</i>
Motion σ_{int}	0.15	0.17	1.34	0.19
Motion n_{samp}	-0.36	-0.63	-5.40	*5.2x10 ⁻⁶
Group	0.1	0.28	2.20	*0.03

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291

292 **Internal noise and sampling**

293

294 To determine whether there was a general trend for group differences in internal
295 noise, a multivariate analyses of variance (MANOVA) was undertaken with one
296 between-participants factor (group at 2 levels: migraine and control) and three
297 dependent variables (orientation, motion and size internal noise) (Fig. 2B). This
298 revealed no main effect of group for internal noise (Wilks' $\lambda=0.85$, $F_{(3,34)}=2$, $p=0.14$,
299 partial- $\eta^2=0.15$). A similar analysis revealed no effect of group on sampling (Wilks'
300 $\lambda=0.86$, $F_{(3,33)}=1.83$, $p=0.16$, partial- $\eta^2=0.14$; Fig. 2C).

301

302 To determine whether group differences existed on a subset of EN tasks, levels of
303 internal noise and sampling were exposed to a series of *post hoc* independent t-tests
304 comparing migraine and control group performances (Table 2). Since analyses were
305 undertaken for all visual dimensions tested (orientation, motion and size), *Bonferroni*
306 corrections were made for three multiple comparisons (corrected alpha level=0.0167).
307 The analyses revealed no significant differences in levels of internal noise or sampling
308 between migraine and control groups for any of the EN tasks.

309 **Predicting coherence thresholds from internal noise and sampling**

310

311 To determine how motion coherence thresholds related to EN performance, bi-variate
312 correlations were undertaken (Fig. 2D&E). Motion sampling was found to be highly
313 negatively correlated with motion coherence thresholds ($R=-0.63$, $p=1.8 \times 10^{-5}$).

314 Participants who were good at global pooling of information in the EN task needed
315 fewer signals dots in the coherence task to correctly classify the direction of signal
316 motion (Fig. 2E). In contrast, motion internal noise did not correlate with motion
317 coherence thresholds ($R=0.22$, $p=0.18$; Fig. 2D).

318

319 Next, a regression analysis was undertaken. This tested the extent to which the three
320 predictor variables [group (migraine or control), motion internal noise, motion
321 sampling] predicted variance in motion coherence thresholds (the outcome variable)
322 (Table 3). The resulting model was highly significant ($F_{(3,34)}=13.3$, $p=7 \times 10^{-6}$) and
323 accounted for 54% of the variance in coherence thresholds ($R=0.74$). Both group
324 (6.6%) and motion sampling (39.44%) variables were found to predict a significant
325 proportion of unique variance in coherence thresholds, whereas internal noise did not
326 (2.4%). These findings indicate that even when differences in levels of internal noise
327 and sampling were factored out, group membership (migraine vs. control) accounted
328 for a significant proportion of variance in coherence thresholds.

329

330 Finally, none of the psychophysical measures recorded (coherence thresholds, internal
331 noise or sampling) correlated with migraine characteristics (Supplementary Table 1).
332 However, we note that the migraine characteristics included were based on self-report
333 (e.g. migraine frequency, duration and severity), and hence, were highly subjective

334 and prone to recall bias. Nor do they capture the fact that the nature of participants'
335 migraines may have changed with time.

336

337 **5. Discussion:**

338

339 In support of previous findings, motion coherence thresholds were elevated in the
340 migraine group relative to the control group. However, this difference could not be
341 attributed to deficits in either local or global processing. EN analysis generated
342 statistically indistinguishable estimates of internal noise (local processing) and
343 sampling (global processing) for migraine and control groups across all three
344 judgements types (orientation, motion and size). Further, regression analysis indicated
345 that group membership (migraine or control) predicted a significant proportion of the
346 variance in coherence thresholds, even once levels of internal noise and sampling
347 were controlled for. As discussed below, these findings are consistent with a relative
348 inability to exclude visual noise in migraine.

349

350 The finding of elevated motion coherence thresholds in the migraine group is
351 consistent with a number of previous reports. Whilst basic judgements of local
352 position¹⁴ and motion¹¹ do not differ between migraine and control groups, repeated
353 studies have shown impaired performance on global form and global motion
354 coherence tasks in which participants must detect global structure embedded in noise^{6,}
355 ^{9, 10, 12-14}. However, it has been argued that so-called 'global' coherence paradigms of
356 this kind do not rely exclusively on global integration processes; instead, performance
357 may also be limited by local processing, i.e. internal noise¹⁵, or the ability to exclude

358 external noise¹⁶. Consequently, EN analysis was undertaken so that independent
359 estimates of local and global processing limits could be obtained.

360

361 The EN analysis undertaken here showed that levels of internal noise did not differ
362 between migraine and control groups across any of the dimensions tested (orientation,
363 motion or size). This is consistent with a number of previous studies. For example, a
364 technique known as the N-pass method²³⁻²⁵, which measures the consistency in a
365 participant's responses to sequential presentations of identical signal plus noise
366 stimuli, has been used to estimate levels of internal noise in migraine²⁶⁻²⁸. The
367 principle underlying the technique is that internal noise reflects the level of random
368 firing in a cell population that is sensitive to the dimension of interest, e.g. the
369 direction of motion. As a result, a participant that is characterised by high internal
370 noise will show poor consistency in responses across sequential presentations, since
371 intrinsic variability in cellular responses, which is independent of the stimulus, will
372 limit performance and drive random responses. Studies using this technique have
373 shown that for global motion²⁸ and two out of three global form tasks tested²⁶⁻²⁸,
374 levels of internal noise in participants with migraine are indistinguishable from those
375 of control participants.

376

377 The EN analyses undertaken here also indicated normal global integration in
378 migraine: levels of sampling were indistinguishable from control participants' for
379 judgements of orientation, motion and size. Although EN analysis has been applied to
380 the study of migraine previously, it has not been used to characterise *visuospatial*
381 performance; instead, previous studies have incorporated judgements of visual
382 *contrast*. Thus, the findings are not directly comparable to our own: contrast EN

383 analysis is different from spatial and motion versions of the task, most pertinently,
384 with respect to the nature of the external noise added to the stimulus²⁹. Consequently,
385 performance is captured by a more complex model that includes additional free
386 parameters including a multiplicative noise term^{30,31}. Nonetheless, two independent
387 studies using contrast EN analysis have reported indistinguishable levels of sampling
388 in participants with and without migraine^{27,32}. Further, they showed that levels of
389 additive internal noise (equivalent to the local noise parameter in the EN model used
390 here) also did not differ between groups. This suggests that the findings we report (i.e.
391 normal local and global processing in migraine) may extend to other (non-spatial)
392 visual dimensions.

393

394 Taken together with previous studies, the data reported here can be reconciled with a
395 simple model of visual processing in migraine that posits normal local and global
396 processing, coupled with a low tolerance to external noise. Thus, performance is
397 seemingly unaffected on tasks that only require integration of the signal (e.g. spatial
398 and motion EN tasks), but is impaired on judgements that first require segregation of
399 the signal from noise (e.g. form and motion coherence tasks). It is noteworthy that a
400 selective deficit in the mechanisms of external noise exclusion has previously been
401 demonstrated in another clinical group characterised by visuo-cortical dysfunction¹⁶.
402 Thus, in amblyopia, performance is reportedly normal on *EN* tasks that involve
403 judgements of global form^{33,34} and motion³⁵, but impaired on related form
404 coherence³⁶ and motion coherence tasks³⁷⁻⁴⁰. Although speculative, the similarity in
405 the pattern of these findings in migraine and amblyopia, coupled with their widely
406 differing aetiologies, raises the possibility that the mechanisms involved in external

407 noise exclusion are particularly vulnerable following cortical damage or cortical
408 reorganisation.

409

410 A number of cortical models of migraine have already been suggested in the
411 literature. The majority of these are based on the notion of abnormal levels of cortical
412 excitation^{4,41}, i.e. *hypo*-excitability (reduced neural activity), or more commonly,
413 *hyper*-excitability (elevated neural activity) relative to healthy controls (see review⁵).
414 Thus, strengthened excitatory connections^{42,43}, impaired mechanisms of inhibition⁴⁴,
415 ⁴⁵ and abnormal pre-activation levels⁴⁶ have all been posited in migraine. However,
416 these models are often poorly specified, such that precise behavioural predictions
417 cannot be made on their basis. For example, hyper-excitability could imply elevated
418 levels of stimulus-driven (i.e. spiking) activity, a specific elevation in base-line firing
419 rates, or else a *generalised* increase in activity, all of which would lead to different
420 predicted effects on the signal-to-noise ratio, and hence, visual psychophysical
421 performance⁵.

422

423 With respect to the current study, the data reported are clearly inconsistent with
424 versions of both the *hyper*- and *hypo*-excitability models that posit an abnormal level
425 of base-line firing rates, since these would predict an elevation or reduction
426 (respectively) in internal noise. Instead, we report normal levels of internal noise in
427 migraine across all three visual dimensions tested (coupled with a selective elevation
428 in motion coherence thresholds). An alternative version of the *hyper*-excitability
429 model, which *is* broadly consistent with these data, is one in which stimulus-driven
430 (spiking) activity is elevated, whilst base-line firing-rates are unaffected. Let us
431 assume that a predominant direction of motion is selected by the observer once a

432 threshold firing-rate is exceeded within a population of appropriately-tuned direction-
433 sensitive neurones: if a single direction of motion is presented, hyper-excitability will
434 increase the likelihood that activity associated with the target direction will reach
435 threshold, and hence be reported. However, for a noisy (e.g. motion coherence)
436 stimulus, a state of hyper-excitability will *also* increase the probability that activity
437 driven by the noise will reach threshold, and hence compete with representations of
438 the signal.

439

440 Consistent with this model of (stimulus-driven) cortical *hyper*-excitability, Antal et
441 al.⁹ demonstrated *superior* motion discrimination performance in migraine (relative to
442 controls) for a stimulus comprised of a single direction of motion (100% coherence),
443 coupled with impoverished (relative) performance once the coherence of the stimulus
444 was decreased (i.e. noise was increased). In an earlier study, Antal et al.⁴⁷ showed that
445 a similar dissociation could also be induced in healthy control participants: following
446 an experimental reduction in the excitability of cortical area MT, the discrimination of
447 intermediate coherence motion was enhanced, whilst the discrimination of 100%
448 coherent motion was impaired. Although we did not find *superior* classification
449 performance in migraine for a stimulus comprised of a single direction of motion
450 (remember that these trials were interleaved with a high noise staircase in the EN task,
451 potentially making the task harder), we *did* find a *selective* impairment in the
452 processing of a noisy (motion coherence) stimulus. Taken together, these data suggest
453 that a dissociation in the processing of motion coherence stimuli and stimuli
454 comprised of a single direction of motion (as reported) *may* be a signature of cortical
455 (stimulus-driven) hyper-excitability.

456

457 In conclusion, the findings reported here are inconsistent with local or global
458 processing deficits in migraine, but instead, implicate impaired mechanisms of visual
459 noise exclusion. This hypothesis has the potential to integrate a wide range of findings
460 from the existing literature and open up novel avenues for investigation. Specifically,
461 it predicts that relative to control participants, people with migraine will be impaired
462 on any visual discrimination or detection task for which signal and external noise
463 must be segregated prior to an integration stage, provided that sufficient external
464 noise is added to the stimulus. Future studies should focus on the mechanisms
465 involved in visual noise exclusion, since little is known about this process. One
466 possibility that has been raised is that impaired noise exclusion reflects a state of
467 (stimulus-driven) cortical hyper-excitability, which increases competition between
468 representations of the signal and the noise. An alternative possibility, which is equally
469 speculative however, is that representations of the noise compete with the signal to a
470 greater extent in migraine because of a failure in endogenous attentional control, i.e.
471 an inability to selectively monitor channels of interest that are most likely to carry the
472 signal^{48,49}. To begin to tease these possibilities apart, it is clear that sophisticated
473 psychophysical techniques must be employed in conjunction with clearly specified
474 models of cortical function, so that highly specific predictions can be tested. We
475 believe that the efficient version of the EN paradigm, which can be adapted to test
476 across multiple sensory dimensions *and modalities*, represents an invaluable tool in
477 this approach.

478

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482 **6. References:**

483

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Supplementary Material

606

607

608 *Equivalent noise analysis*

609

610 The standard equivalent noise (EN) function is of the form:

611

$$\sigma_{obs} = \frac{\sigma_{int} + \sigma_{ext}}{n_{samp}} \quad (1)$$

613

614 where (for motion) σ_{obs} is the participant's offset threshold (i.e. the smallest
615 directional offset from vertical that can be reliably classified), σ_{int} is the participant's
616 additive internal noise, σ_{ext} the external noise in the stimulus, and n_{samp} the effective
617 number of samples that the participant pools to determine the average direction of
618 motion.

619

620 The traditional method of EN analysis constrains (1) by measuring offset thresholds at
621 multiple levels of external noise, typically 6 or more, thereby requiring several
622 thousand trials. However, the novel, rapid method use here, provides reliable
623 estimates of internal noise and sampling in fewer than 100 trials. This rapid EN
624 approach constrains the EN function with just two data-points / staircases (Fig. 1C).
625 The first ('zero noise' condition) involves a manipulation of the signal direction
626 across trials in the absence of noise, such that a basic offset threshold is estimated;
627 this constrains the fit along the ordinate axis. The second ('high noise') condition
628 relies on an inverse manipulation: the mean of the signal is fixed at a high level whilst

629 the level of external noise is manipulated across trials, such that the maximum level of
630 noise that can be tolerated for a given performance level is estimated. This constrains
631 the fit of the model in the orthogonal dimension (along the abscissa), and avoids
632 sampling uninformative regions of the curve.

633

634 *Correction for stimulus wrapping*

635

636 For circular dimensions, i.e. orientation and motion, the stimulus wraps (at π for
637 orientation and 2π for motion). Thus, an orientation of 0° is the same as an orientation
638 of 180° , whilst a direction of 0° is equivalent to one of 360° . Consequently, the
639 standard deviation of a distribution that is sampled to generate noise underestimates
640 the actual variance presented at high noise levels, such that the equivalent noise model
641 predicts lower thresholds in this area of the curve than are actually recorded¹⁵. To
642 overcome this issue we ran Monte Carlo simulations of a model observer's
643 performance across a range of internal noise and sampling levels. These indicated that
644 an observer's sampling level (n_{samp}) is a function of their high noise threshold [i.e. the
645 maximum level of noise that can be tolerated (MTN)] and can be captured by the
646 following equation:

$$647 \quad n_{\text{samp}} = \exp (A\text{MTN}^2 + B\text{MTN} + C) \quad (2)$$

648

649 where best fits are obtained with values for A, B and C of 0.0001, 0.0329 and -1.903
650 for motion, 0.0006, 0.0681 and -1.95 for orientation, and -0.4228, 2.797 and -1.241
651 for size judgements, respectively. Note that these values are specific to a defined
652 threshold performance level (82% here). This simple association between MTN and

653 sampling holds true because at high levels of external noise the effect of internal noise
654 is negligible.

655

656 Once an estimate of sampling has been derived from the MTN, internal noise can be
657 calculated from the 'zero noise' threshold. Thus, when $\sigma_{\text{ext}}=0$, by re-arranging
658 equation (1):

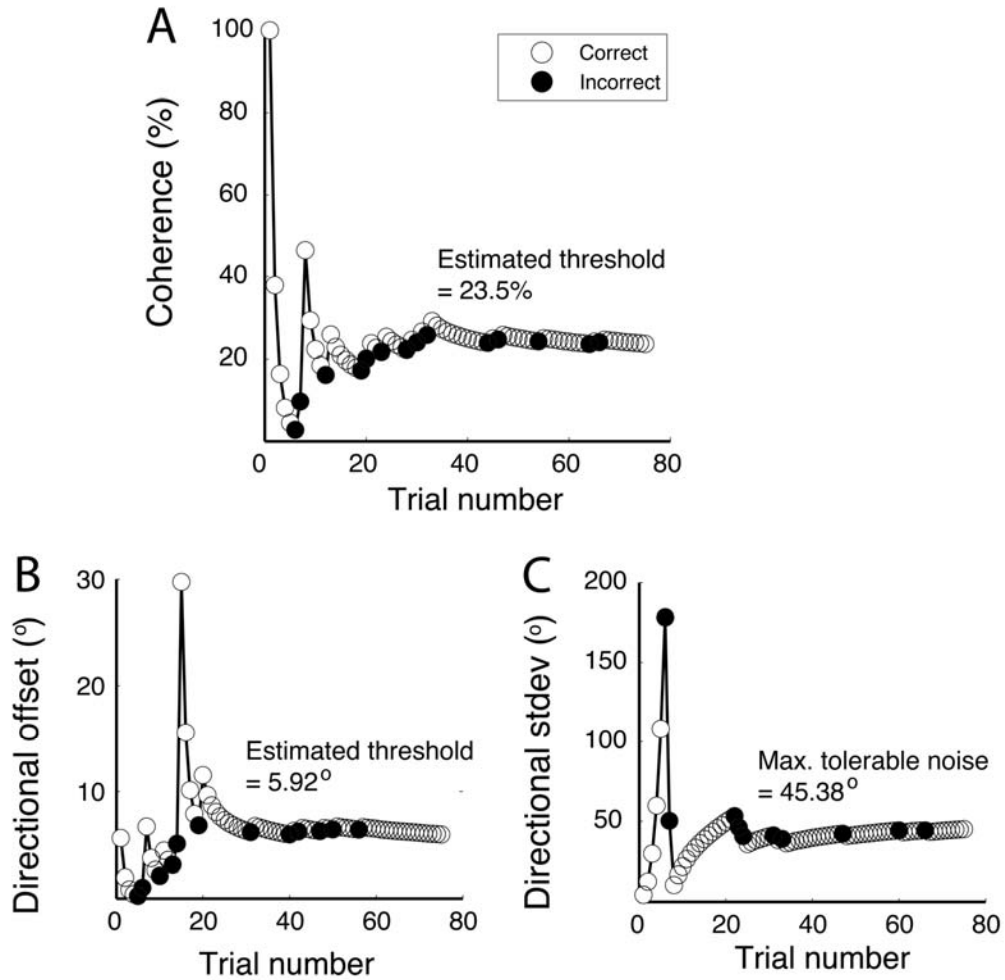
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660
$$\sigma_{\text{int}}^2 = \sigma_{\text{obs}}^2 n_{\text{samp}} \quad (3)$$

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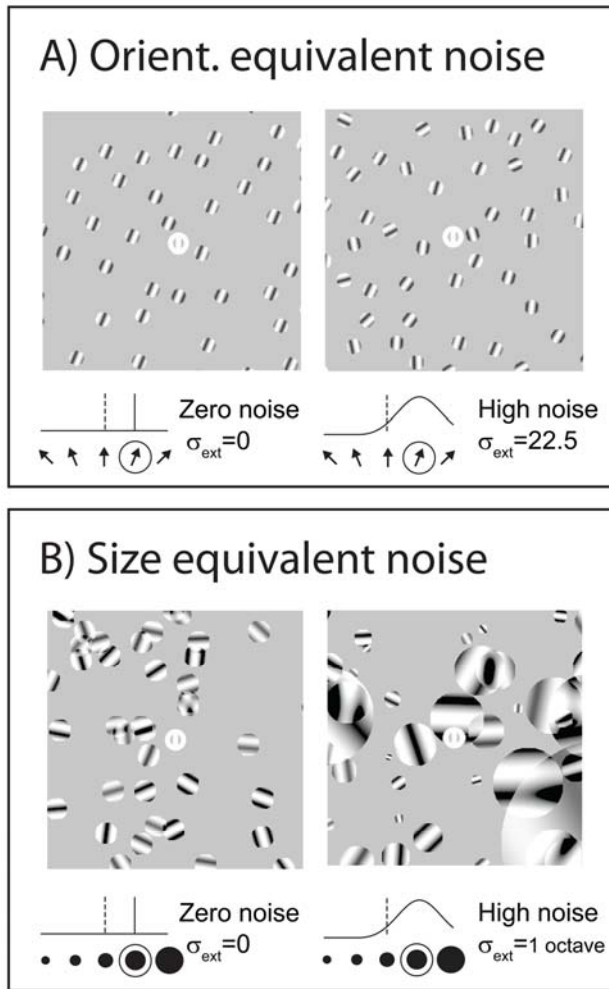
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Supplementary Figure 1. Example staircases. Example staircases are shown for one participant's data for the (A) motion coherence task, (B) motion equivalent noise task (zero noise condition) and (C) motion equivalent noise task (high noise condition). Under the control of QUEST, the stimulus level was set (on each trial) to the most probable Bayesian estimate of the underlying threshold - in this case, the 82% correct threshold.



672

673 **Supplementary Figure 2.** Orientation and size equivalent noise tasks. Example stimuli are shown for
 674 (A) orientation and (B) size equivalent noise tasks with zero noise conditions and high noise conditions
 675 on the left and right, respectively. Underneath each is shown the corresponding distribution of
 676 directions or sizes present in the stimulus. The reference orientation / size is denoted by a vertical black
 677 dotted line; the average signal orientation / size is circled.
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Supplementary Table 1. Correlations between psychophysical measures and migraine characteristics. Pearson's correlation coefficients (*R*) and associated significance levels (*p*) are reported. Th=motion coherence threshold; σ_{int} =internal noise; n_{samp} =sampling.

			Age	Onset	Freq1	Freq2	Last	Duration	Severity
Coherence	Th	R	-0.06	0.36	-0.19	-0.17	-0.02	-0.13	-0.31
		p	0.74	0.11	0.45	0.46	0.93	0.57	0.18
Orientation	σ_{int}	R	-0.19	0.37	-0.11	-0.14	0.17	-0.09	-0.28
		p	0.23	0.09	0.63	0.54	0.45	0.67	0.20
	n_{samp}	R	-0.07	-0.04	-0.28	-0.14	0.13	-0.06	0.01
		p	0.66	0.86	0.25	0.56	0.56	0.78	0.96
Motion	σ_{int}	R	0.08	0.00	0.12	0.15	-0.08	0.33	0.24
		p	0.63	0.99	0.60	0.49	0.71	0.13	0.29
	n_{samp}	R	0.09	-0.30	0.28	0.21	0.04	-0.12	0.32
		p	0.57	0.18	0.24	0.35	0.87	0.58	0.15
Size	σ_{int}	R	-0.17	-0.06	-0.17	-0.20	0.37	-0.37	-0.12
		p	0.30	0.79	0.49	0.38	0.09	0.10	0.60
	n_{samp}	R	-0.14	-0.03	-0.05	-0.11	0.22	-0.18	-0.05
		p	0.40	0.91	0.84	0.65	0.36	0.46	0.84