Evidence for Distinct Clusters of Diverse Anomalous Experiences and Their Selective Association with Signs of Elevated Cortical Hyperexcitability

[1]Chun Yuen Fong*

[2]Chie Takahashi

[3]Jason J Braithwaite

[1] Behavioural Brain Sciences centre, School of Psychology, University of Birmingham, UK, B15 2TT.

[2]School of Computer Science, University of Birmingham, UK, B15 2TT.

[3] Department of Psychology, Lancaster University, UK, LA1 4YF.

*corresponding author:

Email: tcf479@bham.ac.uk (Chun Yuen Fong)

1. Introduction

Aberrant excitation in the cerebral cortex has long been associated with the formation of both elementary and complex hallucinations (Elliott, Joyce, & Shorvon, 2009; Ffytche et al., 1998; Manford & Andermann, 1998; McGuire, Murray, &, Shah, 1993; Panayiotopoulos, 1994; Sass & Parnas, 2003). For example, patients who have been diagnosed with complex partial seizures of the temporal lobe, migraine with aura, and schizophrenia will commonly report a host of auric hallucinatory experiences – and all these conditions / disorders are associated with increased and excessive neural activity (see Abraham & Duffy, 2001; Dahlem & Muller, 2003; Dahlem, Engelmann, Lowel & Muller, 2000; Hadjikhani et al., 2001; Lauritzen, 2001; Leão, 1951; Merabet, Kobayashi, Barton & Pascual-Leone, 2003; Salanova, Andermann, Oliver, Rasmussen, & Quesney, 1992; van den Maagdenberg et al., 2004; Weiss & Heckers, 1999).

Neurological studies have supported the association between the underlying degree of visual cortical hyperexcitability and resultant aberrant experience (Abraham & Duffy, 2001; Dahlem & Muller, 2003; Salanova et al., 1992; Weiss & Heckers, 1999). Previous studies utilising transcranial magnetic stimulation (TMS) protocols have shown that migraineurs with aura had a lower phosphene threshold relative to non-migraine control groups and migraineurs without aura (Aurora et al., 1999; Aurora, Welch, & Al-Sayed, 2003; Aurora & Wilkinson, 2007; Fumal, Bohotin, Vandenheede, & Schoenen, 2003). In addition, the amplitude of visually evoked potentials (VEPs) has been shown to be greater in migraine populations relative to control groups (Connolly, Gawel, & Rose, 1982; Shibata, Osawa, & Iwata, 1997) and neuroimaging studies have demonstrated that the phenomenological content of aura varies in sympathy with the rate and range of cortical spreading depression in sensory cortex – providing a direct link between the presence of hyperexcitable states and visual hallucination / aura (Hadjikhani et al., 2001). Collectively, these findings support the view

that cortical hyperexcitability is an underlying contributing factor for predisposition to anomalous experience.

1.1 Trait-based Questionnaires to quantify Cortical Hyperexcitability

One approach to quantifying cortical hyperexcitability via the symptoms associated with it, has been to use trait-based questionnaires / screens. However, many of them were based primarily on intuition, had not been formally explored or validated via factor analysis, or had not been fully explored in relation to other more direct state-based measures. Examples would include the Meares–Irlen (MI) Scale (Hollis & Allen, 2006; Irlen, 1983) and the Visual Discomfort Scale (VDS: Conlon, Lovegrove, Chekaluk, & Pattison, 1999). The former measure utilised a basic yes / no response to a small number of questions and the latter had a poor question structure making it problematic to interpret which anomalous perceptions were being endorsed (see Braithwaite, Marchant, Takahashi, Dewe, & Watson, 2015a for further discussion).

More recently Braithwaite and colleagues (2015a) were the first to use exploratory factor analysis (EFA) to produce a verified indirect proxy measure of cortical hyperexcitability – termed the Cortical Hyperexcitability index, or '*CHi*'. The EFA produced a 3-factor solution suggesting that the different items / experiences may reflect a non-unitary notion of cortical hyperexcitability. While an important development, the resulting 3-factor solution had an unexpected and not entirely intuitive structure in that it divorced both positive and negative hallucinatory experiences onto separate, though correlated, factors. In addition, a number of items did not survive the EFA process and were dropped from the final index.

1.2 "Pattern-glare" PG Task to reflect State-based Cortical Hyperexcitability

One behavioural paradigm used to quantify state-based cortical hyperexcitability is the *"pattern-glare"* (PG) task. Viewing striped gratings with a spatial frequency of approximately three cycles-per-degree of visual angle, can be highly irritable to observers, can induce increased visual stress (eye strain/visual pain) and cause the perception of phantom visual distortions (Evans & Drasdo, 1991; Wilkins, 1995; Wilkins & Nimmo-Smith, 1984; see Evans & Stevenson, 2008, for a review). Pattern-glare refers to a host of phenomena (visual distortions, illusions, nausea, dizziness, etc) that are induced from viewing these aversive visual stimuli (Evans & Stevenson, 2008; Wilkins, 1995; Wilkins et al., 1984).

One account proposed for the occurrence of these phenomena is that potent gratings over-stimulate localised groups of visual neurons causing them to fire inappropriately - the increased likelihood of which is thought to reflect an elevated degree of cortical hyperexcitability. It follows that susceptibility to such visual distortions should vary in sympathy with, and reflect, elevated degrees of latent cortical hyperexcitability. In line with this view, elevated degrees of pattern glare are associated with migraine with aura (Aurora & Wilkinson, 2007; Friedman & De Ver Dye, 2009; Haigh, Karanovic, Wilkinson, & Wilkins, 2012; Harle & Evans, 2004; Huang, Cooper, Satana, Kaufman, & Cao, 2003; Oelkers et al., 1999; Wilkins, 1995, 1984), with visual stress (Meares-Irlen (MI) syndrome: Evans, Busby, Jeanes, & Wilkins, 1995; Evans & Stevenson, 2008), photosensitive epilepsy and stroke (Beasley & Davies, 2012; Evans & Stevenson, 2008; Harding & Fylan, 1999; Harding, Harding, & Wilkins, 2008; Wilkins, 1986; Wilkins, Binnie, & Darby, 1980; Wilkins et al., 1984; 1980) and certain hallucinations in the non-clinical population (Braithwaite, Broglia, Bagshaw, & Wilkins, 2013).

In addition, neuroimaging studies have demonstrated significantly increased Blood Oxygenation Level Dependent activation in visual association cortex but only for migraineurs with aura and only for the presentations of the critical irritable stimuli (and not baseline gratings: Huang et al., 2003; Huang et al., 2011). Furthermore, the degree of visual distortion experienced by observers has been shown to correlate with the level of neural activities in the visual association cortex (Datta, Aguirre, Hu, Detre, & Cucchiara, 2013; Welch, Bowyer, Aurora, Moran, & Tepley, 2001) and there is evidence from near infrared spectroscopy (NIRS) to suggest that migraineurs' brain generates faster neural responses to the irritable gratings (relative to controls: Coutts, Cooper, Elwell, & Wilkins, 2012). Collectively, these findings indicate a relationship between aberrant neural processes (brain-imaging) and anomalous experience (pattern-glare) and support the usage of the PG task as an index for cortical hyperexcitability.

1.3 The Present Study

The present study aimed to provide evidence that our revised and improved proxy screening measure of cortical hyperexcitability (a newly modified *CHi-II*) can reflect a more intuitive factor structure than that seen previously. Irrespective of the previous literature discussed, there is currently only one validated proxy trait-based measure to quantify the symptoms associated with cortical hyperexcitability and its role underlying different forms of aberrant experience. We believe that the availability of such useful screening measure for cortical hyperexcitability could have great utility for scientific, clinical and neuroscientific research. As well as revealing interesting clusters of experiences in its own right, such a measure can be inexpensive and straightforward to implement – making it a pragmatic approach for many scientific and clinical investigations. If supportive evidence is found in the present study, this newly modified *CHi-II* could act as a covariate alongside neuroscientific methods such as neuroimaging, brain-stimulation, and electroencephalography helping to

bridge the explanatory gap between aberrant neural processes and resultant anomalous experiences of a specific type or theme.

To achieve our aim, we have designed two experiments with different research regimes conducted on independent participant groups, that sought to identify key factors associated with cortical hyperexcitability in Study 1 (*CHi-II* on healthy controls), which were then tested for supporting evidence in Study 2 (PG task and *CHi-II* on healthy controls and migraineurs). Specifically, we expected that the EFA in study 1 would reveal some stable and clear factors representing separate but inter-correlated dimensions that the *CHi-II* could be broken down into. Then in the second study, we evaluated the utility of *CHi-II* as a proxy measure of cortical hyperexcitability by exploring its relationship with a computer based PG task and with a migraine group. If each factor represents diverse neurocognitive contributions to the concept of visual cortical hyperexcitability, then selective correlations might exist between the *CHi-II* factors and more objective and established computer-based assessments of symptoms reflecting cortical hyperexcitability.

In general, we hypothesized that in Study 2, the participant groups which are known to have an increased degree of cortical hyperexcitability (migraineurs & some non-clinical subjects) will score higher on the *CHi-II* items that belong to the identified factors revealed to be linked with visual aberrant experiences in Study 1. As well as any resultant factor structure being informative, it was predicted that not all factors might be reliably associated with cortical hyperexcitability – as some aberrant perceptions may reflect more pre-cortical / ocular processes (Conlon et al., 1999). Knowing which experiences cluster onto related factors and which factors would then be associated with elevated pattern-glare scores, and for a migraine-group, would significantly expand our understanding and provide a truer representation of cortically mediated processes. This paper will first introduce an overview, methods and the analysis for Study 1, then Study 2, followed by reporting the results from

both studies, leading into a general discussion where the findings and implications from both studies are discussed.

2. Methods

2.1 Study 1 – EFA on a modified *CHi-II* with non-clinical participants

In Study 1, we constructed the Cortical Hyperexcitability index – II (*CHi-II*), which is a revised version of the original Cortical Hyperexcitability index (*CHi*) with several methodological amendments. First, some poor loadings or non-loadings from the original study were removed from the measure. Second, some items were modified with more detailed and specific descriptions added, for certain anomalous visual experiences. Third, more items relating to elementary hallucinations and distortions were added. Finally, an exploratory factor analysis (EFA) was conducted on a new large independent group of non-clinical participants in order to uncover the latent structure of the *CHi-II*.

2.1.1 Participants

Three hundred participants from the University of Birmingham were recruited to participate in the study (T1). Of these, 232 (54.0%) returned 14 – 35 days later (T2) to explore the test-retest validity of the *CHi-II* measure. The mean age of the participants was 19.5 (age range 17-40 years), of which 258 (86%) were female, 268 (89.3%) were right-handers. All participants received either research credits or a small financial payment in return of their participation. All participants were given a pre-screening questionnaire prior to their participation in the experiment. The questions included whether the subjects had (i) any ocular conditions (e.g. astigmatisms/colour blindness/optic neuritis/accommodation errors), (ii) ever undergone any form of neurosurgery (including eye surgery), (iii) been diagnosed with migraine (with or without aura / hallucination), (iv) been diagnosed with epilepsy (with

or without aura / hallucination) or seizures of unknown origin, (v) ever suffered from neurological conditions / disorders (and whether they were taking medication as a form of treatment), (vi) ever suffered from a psychiatric condition (and whether they were taking medication as a form of treatment). Participants who gave a positive response to any of the listed questions were excluded from the study. Informed consent was obtained for all the participants.

2.1.2 Cortical Hyperexcitability index - II (*CHi-II*)

The *CHi-II* was composed of 30 items, of which 16 were original *CHi* items. Eight items were either adapted from the Cardiff Anomalous Perception Scale (*CAPS*; Bell, Halligan, & Ellis, 2005), the Cambridge Depersonalization Scale (*CDS*; Sierra & Berrios, 2000), the Meares-Irlen scale (*MI*; Hollis & Allen, 2006) or the Visual Discomfort Scale (*VDS*; Conlon et al., 1999) and 6 items were completely new. In addition, 11 items were modified with more details to make them more specific and precise. The last modification was the removal of 5 items from the original *CHi* questionnaire, because they loaded poorly onto the original factor structure of *CHi* (see Braithwaite et al., 2015a; see Table 1.).

Each item of the *CHi-II* contained a question about a specific experience followed by two 7-point unipolar Likert scales to measure participants' corresponding 'frequency' (0 = never and 6 = all the time) and 'intensity' (0 = not at all and 6 = extremely intense) of such experiences[1]. The ratings of frequency and intensity for each question were summed to provide a score for that item (max. = 12). The index for a subject's cortical hyperexcitability is the arithmetic sum of scores for all 30 items (max. score = 360).

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[1] In the original *CHi,* the response scale ranged from 1 to 7 because it was not clear whether a zero value would be treated the same as the other non-zero values. Subsequent pilot testing has demonstrated that this is not an issue for the current measure.

Table 1. Table showing the item change of CHi-II compared to CHi and the source of the questions.

Question	Change compared to CHi	Source
1) Vision more sensitive to external sensory information?	Same	CHi original item
2) Overwhelmed by visual information?	Same	CHi original item
3) Visual perception seems heightened or enhanced?	Same	CHi original item
4) Irritation from indoor lights?	Modified	CHi original item
5) Everyday objects look different?	Modified	Adapted from CAPS/ CDS
6) Ever experienced transient flashes or spots of white light?	Modified	CHi original item
7) Find certain environments irritating?	Same	CHi original item
8) Ever seen fleeting shapes?	Split from Q8.	CAPS item
9) Ever experienced flashes of colour?	Split from Q8.	CAPS item
10) Find the appearance of things or people changes?	Modified	CAPS item
11) Felt dizzy / nauseous due to strong light or patterns?	Same	CHi original item
12) Lights or colours seem brighter or more intense?	Same	CAPS item
13) Experienced visual discomfort from certain patterns?	Modified	CHi original item
14) Had a headache / migraine induced by visual information?	Same	CHi original item
15) Experienced visual distortions when you look around?	New	New
16) Working on computer for long periods irritates eyes?	Modified	Adapted from MI
17) Noticed perceptual distortions when you are fatigued?	Modified	CHi original item
18) Fluorescent lights irritate your eyes?	Modified	Adapted from MI & VDS
19) Had an out-of-body experience?	Modified	CHi original item
20) Headlights from oncoming traffic irritate eyes?	Modified	Adapted from MI
21) Experienced visual discomfort from reading?	Same	CHi original item
22) Experienced a narrowing of your visual field?	Same	CHi original item
23) Experienced flashes of moving patterns?	Modified	CHi original item
24) Experienced loss of visual information?	Split from Q24.	CHi original item
25) Ever seen white/black dots across your visual field?	New	New
26) Ever seen coloured shapes, balls or patterns?	New	New
27) Ever had loss of vision surrounded by zigzag patterns?	Split from Q24.	CHi original item
28) Ever experienced spiral, tunnel or funnel-like shape?	New	New
29) Ever experienced 'spider-web' patterns?	New	New
30) Experienced the world draining in colour and vibrancy?	New	New

2.1.3 Analysis

To uncover the factor structure of the *CHi-II*, an Exploratory Factor Analysis (EFA) was conducted in Study 1, complemented with a parallel analysis (PA: Hayton, Allen, & Scarpello, 2004; Horn, 1965). Two multivariate normality (MVN) tests were conducted separately by the "psych" and "MVN" package installed under the R statistical program (version 3.3.2, R Development Core Team, 2016; see Revelle, 2014; Korkmaz, Goksuluk, & Zararsiz, 2014). The reliability of the scale was based on the internal consistency (Cronback's alpha) and the test-retest reliability (correlations between T1 and T2).

2.2 Study 2 - PG task and modified *CHi-II* with Controls and Migraineurs

Study 2 aimed to explore further the utility of the new *CHi-II* measure, and its factor structure, in relation to the concept of cortical hyperexcitability and its relationship to aberrant visual experiences. The development of *CHi-II* was based on the notion that cortical hyperexcitability could be considered as a continuum, where a stronger background (trait-based) level of cortical hyperexcitability would lead to a higher frequency and intensity to some forms of anomalous visual perceptions. As a result, if both *CHi-II* and the pattern-glare effect reflect cortical hyperexcitability there should be a positive relationship between the trait-based measure (*CHi-II*) and the state-based behavioural measure (i.e. the PG task) not just among migraineurs but also in the non-clinical populations.

Aberrant perceptions, hallucinations and delusions can often co-occur and can be seen collectively in psychosis, schizophrenia and broader neurological conditions and disorders (Yung et al., 2009; Verdoux & van Os, 2002). Such co-occurrence has also been documented for non-clinical groups in the absence of any salient pathology or disorder (Allen et al., 2010; Freeman & Garety, 2003; Lataster et al., 2006). For the present purposes it becomes useful and prudent to ensure, as much as possible, that the *CHi-II* and our PG task tap into the

mechanisms underlying aberrant perceptions and not aberrant beliefs or delusions. Aberrant beliefs could be present and mediating responses, to some degree, on PG tasks where participants are simply biased to responding positively and hence elevating responses to all gratings.

Therefore, to examine that our factors of interest are indeed more related to valid measures of anomalous perceptions and do not reflect strong contaminations from anomalous beliefs, in Study 2 we also administered a questionnaire measure to quantify predisposition to anomalous beliefs. To do this, the Community Assessment of Psychic Experiences (CAPE: Stefanis et al., 2002), which was designed to measure the psychosis proneness of the general population by their symptomatic thoughts, feelings, impressions and beliefs, was administered.

The effects from the newly devised *CHi-II* and the pattern-glare task should be specific to proxy measures of cortical hyperexcitability that underlie anomalous perceptions (and perhaps only some of the factors relative to others) but should not be related to other trait measures of aberrant beliefs (thus also controlling for aspects of suggestion and response bias which are common in hallucinators with psychosis / schizophrenia: Yung et al., 2009; Verdoux & van Os, 2002) . Therefore, Study 2 explored how the factors of the *CHi-II* measure were selectively associated with pattern-glare assessments of cortical hyperexcitability and how pattern-glare was associated with measures of additional aberrant beliefs and not just aberrant perceptions.

Study 2 was conducted with both self-reported migraineurs and non-clinical participants. First, the PG effect and the scores of *CHi-II* between migraineurs and the controls were compared. Second, participants with high PG effect were compared with those with lower PG effect based on their *CHi-II* scores. However, correlations on behavioural

responses could also be driven by response style to questionnaires (Lee, Jones, Mineyama, & Zhang, 2002). For example, if a group of participants tended to give more extreme responses, we would expect them to consistently do so throughout all the measures. As a result, a high score in *CHi-II* would often come with more associated visual distortions (AVD) regardless of any visual cortical activities. To reduce such an effect coming from response bias we used heightened responses to the low-frequency grating as exclusion criteria. In addition, a subtraction parameter of AVD (between high frequency and medium frequency), instead of AVD of medium frequency alone, was used as a measure of PG effect. Furthermore, an additional trait measurement of aberrant beliefs (which are not thought to be driven directly by cortical hyperexcitability occurring in early sensory areas: Community Assessment of Psychic Experiences) was administered.

In Study 2, we hypothesized that; (i) migraineurs would score higher on the *CHi-II* measure and show evidence of higher cortical hyperexcitability via the PG task compared to the control group; and that, (ii) control participants who produce elevated scores on the PG task would also be associated with higher *CHi-II* scores (and perhaps only for some of the factors). Such observations should neither be found in the migraineurs nor the high-scoring PG non-clinical group for the Community assessment of psychic experiences (*CAPE*) measure.

2.2.1 Participants

A total of 354 participants took part in Study 2. Of these, 300 had also taken part in Study 1. In addition, for the present study, 54 new participants were recruited and 27 of them were self-declared migraineurs (10 without aura and 17 with aura) whom were not taking any prophylactic medications. The attack frequencies of the migraine sample ranged from weekly to yearly basis. All the migraineurs were free from attack for at least 7 days before taking part

in the experiment. All participants gave full informed consent to the experiment. Eleven

subjects were rejected at the end (reasons were explained in the result section), which gave a

final sample size of 343. Control participants reported no general conditions of headache as

such factors may still reflect different forms of migraine or other forms of headache.

The mean age of this sample was 19.6 (range = 17 – 40). Among the subjects, 296

(86.3%) were female, and 306 (89.2%) were right-handed. All subjects were given a pre-

screening questionnaire prior to their participation. Subjects who reported that they (i) had

undergone any neurosurgery (included eye surgery), (ii) had any form of history of epilepsy

(or seizures of unknown origin) were excluded from the study, (iii) had ever suffered from

any neurological conditions (other than migraine), and taken medication as treatment, or (iv)

had ever suffered from psychiatric conditions (and taken medication as treatment) were

excluded from the study. Normal or corrected to normal vision without visual impairment had

been self-reported by all participants.

2.2.2 Materials and Procedures

2.2.2.1 The Pattern-glare task. The computerized pattern-glare (PG) task was a modified

version of that reported previously (Braithwaite et al., 2015b; Braithwaite et al., 2013a,

2013b; Evans & Stevenson, 2008). The main modifications came in the form of a more

sensitive Likert-type response for each distortion reported which now depicted the actual

'intensity' of the perceived distortion rather than just its mere presence. The PG task consisted

of presenting three square-wave achromatic elliptical gratings that differed only in terms of

their respective spatial frequency (cycles-per-degree: cpd). The three frequencies were: a

baseline low frequency grating (LF) of 0.5cpd, the crucial medium frequency grating (MF) of

3cpd, and a baseline high frequency grating (HF) of 15cpd (see Figure 1 for an example of

the grating). Each grating was presented three times in a pseudo-random order. A restriction

was programmed into the task so as not to present the same grating twice in a row.

All gratings had a Michelson contrast of 0.70 (cd/m^2). The screen background

luminance was 20 cd/m^2. Gratings were presented in the centre of a 16-inch Samsung

SyncMaster 793DF computer screen (60Hz refresh rate and 1280x960 pixels screen

resolution) using E-prime v2.0 software. The stimuli had a maximum height x width of 120

mm x 155 mm with the shape of a mild ellipse. The viewing distance was fixed and set at 80

cm from the screen, which provided a visual angle of 8.53 x 11.0 degrees.
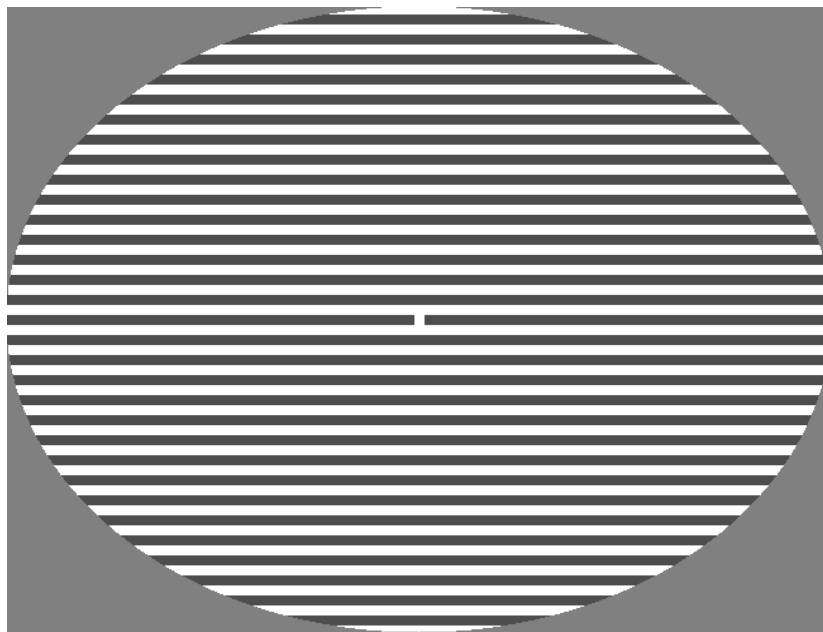

 Figure 1. An example of the highly irritative medium frequency square-wave pattern-glare

stimuli, used in the present study.

Every trial started by presenting one of the three gratings. Participants were told to

focus on a centrally located fixation point on the grating. Participants also were informed that

if the grating / stimuli was too uncomfortable to look at, that they could press the 'spacebar'

button, which removed the stimulus from the screen (repressing made it return). Spacebar

presses were also counted and recorded by the computer programme as an additional

measure. The individual stimuli remained on the screen for a viewing period of 12-seconds

and then removed from view. After an inter-stimulus interval of 1 second, participants were

then presented with a screen that posed a series of questions pertaining to different distortions

(which we termed associated visual distortions: AVDs) and a 7-point Likert scale response

pertaining to the intensity/ strength of the individual AVD that was experienced (0 = not at

all, 6 = extremely; see figure 2. for the trial sequence).
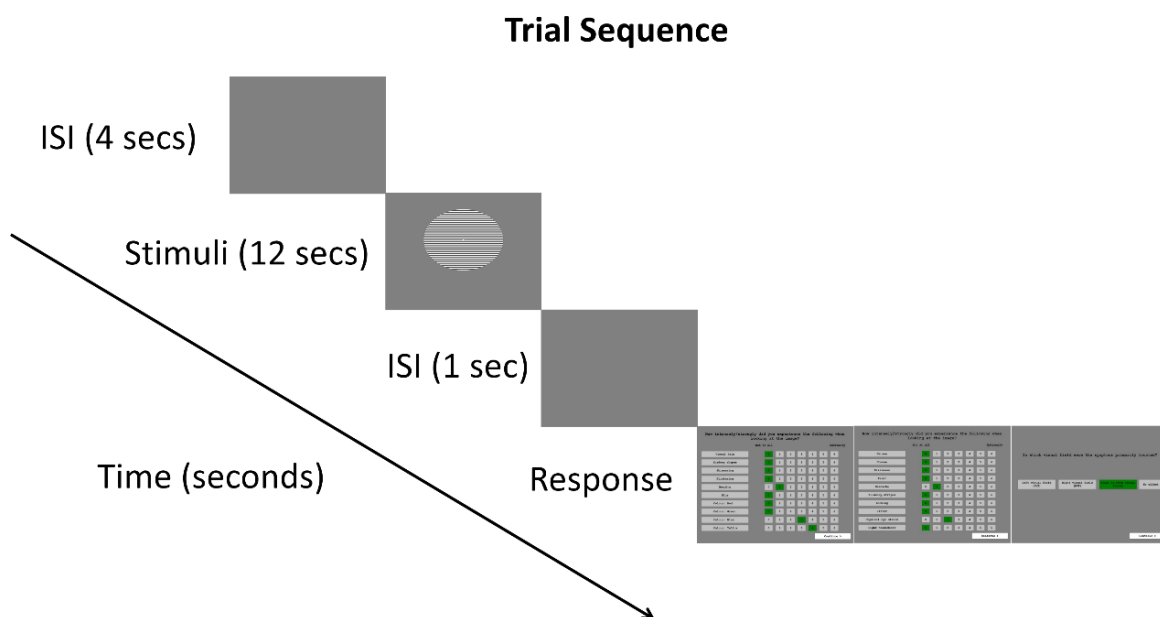
Trial Sequence

Figure 2. A trial sequence for the PG task

A response of zero was taken to indicate that the participant did not experience that

distortion while viewing the grating. Any non-zero response was taken to indicate the

presence of that distortion, at the intensity indicated. Twenty AVDs were provided across two

separate screen presentations which participants completed at their own pace. These Likert

responses, for each AVD, were then summed for that particular grating (range = 0 – 120).

Participants were then also asked to rate whether the AVDs were experienced more in the left

visual field (LVF), the right visual field (RVF), both visual fields or not at all. Individual

trials (for each grating) were separated by an inter-stimulus interval of 4 seconds before the

next trial and questions were presented (see Table 2).

Table 2. The set of questions that being asked after each presentation of a PG stimulus.

Questions	Responses
How strong/intense are the following when looking at the pattern?	0, 1, 2, 3, 4, 5, 6 (0 denoted as not at all and 6 denoted as extremely)
1. Visual pain, 2. physical eye strain, 3. Unease 4. Nausea 5. headache, 6. dizziness, 7. light-headedness, 8. faint	
9. Shadowy shape, 10. Illusory stripes, 11. Shimmering, 12. flickering, 13. jitter, 14. Zooming 15. blur, 16. bending of lines, 17. Red, 18. green, 19. blue, 20. yellow	
Are the effects mainly in the	Left visual field (LVF) Right visual field (RVF) About the same in both visual fields No effect

A practice trial was given to the participants prior to the actual experiment to make

sure that they understood the task, the nature of the AVD questions, and how to provide

responses. This practice trial used a low-frequency checkerboard (0.5cpd) stimulus, which

was not irritating to view. The experiment was carried out in a dimly lit laboratory. The task

itself took approximately 15 minutes to complete, and the whole experiment (including the

completion of questionnaires and screening criteria) took 40 minutes.

2.2.2.2 Questionnaire measure. Participants completed 2 questionnaires that sought to

measure trait-based predisposition to anomalous perceptions or anomalous beliefs. These

measures were: (1) our new Cortical Hyperexcitability Index-II (*CHi-II*), and (2) the

Community Assessment of Psychic Experience (*CAPE*; Stefanis et al., 2002). All the

questionnaires were digitized, programmed (in *Microsoft Access 2013)* and presented on

computer.

 2.2.2.2a *Cortical Hyperexcitability index – II (CHi-II).* From the results of Study 1, the three factors of the *CHi-II* were explored separately in relation to the pattern-glare task. The version of *CHi-II* being used in this study consisted of the 26 items that survived in the EFA from Study 1. Both frequency and intensity were summed for each question (providing a score of 0 – 12 for that item), which gives a maximum overall score of 312.

2.2.2.2b *Community Assessment of Psychic Experiences (CAPE).* To measure a component of belief rather than perception, and also control for suggestibility in our subjects, the *CAPE* questionnaire measure was administered. The *CAPE* is a 42-item self-reporting assessment for schizotypal symptoms built on a 3-dimensional model proposed by Stefanis and colleagues (2002). The three dimensions are *positive symptoms (POS)*, *depression symptoms (DEP)* and *negative symptoms (NEG)*. Each item consists of two 4-point scales (0-3) to represent the symptom frequency ('never', 'sometimes', 'often', 'nearly always') and level of distress ('not distressed', 'a bit distressed', 'quite distressed' and 'very distressed') caused by that experience. Adding up the scores of every item gives an overall index in a maximum score of 252. Although the *CAPE* does have some questions that might pertain to anomalous perceptions, the vast majority of questions pertain more to beliefs, thoughts, impressions and feelings. If elevated pattern-glare scores reflect response biases, then these biases should be present in the *CAPE* measure, predicting a positive correlation between CAPE and PG scores.

3. Results

3.1 Results of Study 1

3.1.1 Descriptive Statistic

The overall mean score of *CHi-II* was 64.6 (median = 58.0), with a standard deviation of 36.6 (range = 2-201). The *CHi-II* score distribution was moderately right skewed, with a

skewness of .811, (*S.E* = .141) but a negligible Kurtosis of .587 (*S.E* = .281). To further

examine the normality of the total score, a Shapiro-Wilk test was conducted which suggested

a non-normal distribution, *W* = .956 (df = 300), *p* < .001 (which is to be expected for a

measure that may reflect multiple factors).

3.1.2 Factor extraction method

The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy number of factors

was .88 and the Bartlett's Test of Sphericity was also significant (χ^2 = 2840 (df =435), p

< .001), which both justified the factorability of the current data set (Kaiser & Rice, 1974;

Tabachnik & Fidell, 2007; Williams et al., 2009).

In order to construct a model and generate different dimensions to represent the

current variables in *CHi-II*, conducting an Exploratory Factor Analysis (EFA) instead of

Principal Component Analysis (PCA) is a more reliable option to uncover the latent structure

of *CHi-II* (Conway & Huffcutt, 2003; Fabrigar, Wegenerm, MacCallum, & Strahan, 1999;

Henson & Roberts, 2006; Widaman, 1993; Williams, Onsman, & Brown, 2009). The

Principal Axis Factoring (PAF) method of factor extraction is a better choice if the data

violate the assumption of multivariate normality (MVN; see Costello & Osborne, 2005;

Fabrigar et al., 1999). The result of Mardia's MVN test and Royston's MVN test both

suggested that the data did not follow a multivariate normal distribution (multivariate

skewness = 352, p < .001; multivariate kurtosis = 1384, p < .001; *H* = 2579, p < .001),

therefore the use of PAF was justified (see Korkmaz, Goksuluk, & Zararsiz, 2014 for a R

package guide for MVN's test).

3.1.3 Rotation Methods

The goal of rotating the factors is to achieve a simple and interpretable structure that

attempts to have each variable saliently loaded ($\geq$ 0.4) onto only one of the extracted factors

but poorly loaded (< 0.1) onto any other factors (Brown, 2009; Yong & Pearce, 2013). The

previous study on *CHi* showed that all the extracted factors correlated with each other

significantly (all r > 0.5; Braithwaite et al., 2015a), which supports the usage of oblique

Promax rotation instead of orthogonal solutions (see Fabrigar et al., 1999; Hendrickson &

White, 1964; Williams et al., 2010).

3.1.4 Number of Factors to extract

Initially, a visual analysis of the Scree Test implied a 4-factor model (Cattell, 1966).

However, a more objective parallel analysis (PA) for PAF was also conducted (see Figure 3

for the scree plot). A set of random factors was generated using Monte-Carlo simulations

with the same number of variables and sample size compared to the data set (Horn, 1965;

Ledesma & Valero-Mora, 2007). The factors from the actual data set with higher eigenvalues

than the simulated one were retained. To reduce the over-extraction problem of PA, alpha

was set at 0.01 (99% percentile; Glorfeld, 1995). As a result, 5 factors were obtained.

Therefore, the 5-factor model (from PA) together with the 4-factor model (form the Scree

Test) were both explored. However, neither the 4th factor nor the 5th factors had more than

three items loading onto them, making them unstable and unreliable, hence justifying the

removal of them from the final model (see Beavers et al., 2013; Costello & Osborne, 2005).
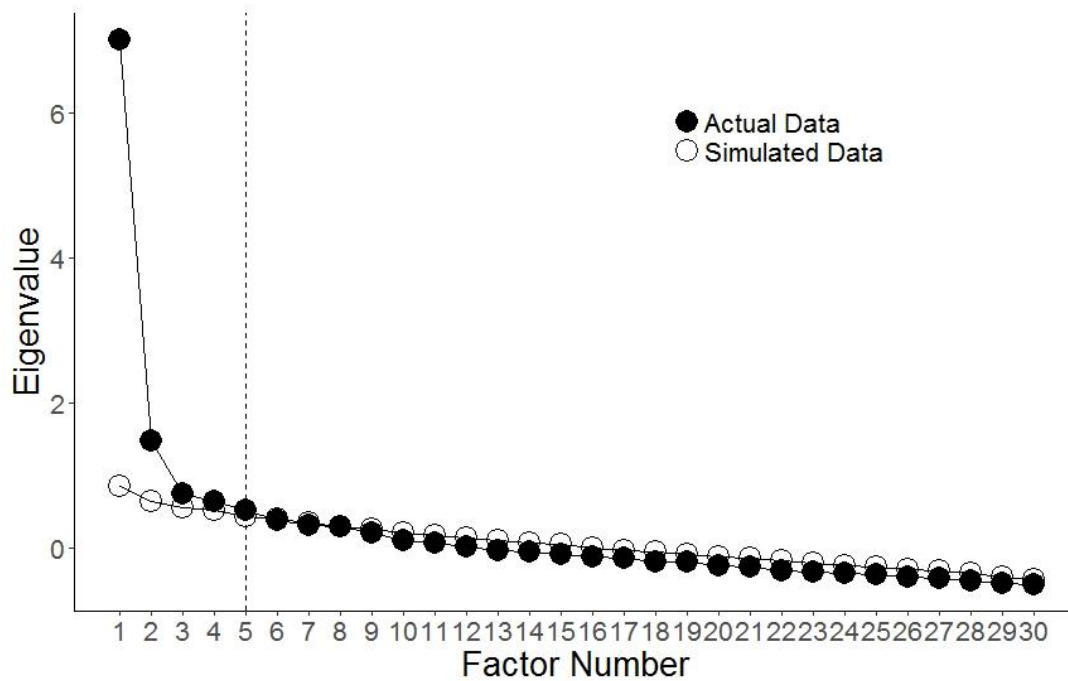
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Figure 3. A parallel analysis scree plot of the PAF suggesting that 5 factors should be retained.

3.1.5 Final Model

As a result, 3 factors were extracted using the Principal axis factoring with the rotation method set as Promax with a kappa of 4. The Promax rotation converged within 6 iterations. The finalized 3-factor model explained 38.6% of the variance and 31.9% after extraction (See Table 3 for the factor structure). The items without any loadings of .40 or above were dropped (Tabachnick & Fidell, 2014). Four items failed to meet this criterion (*Question 2. Do you ever feel overwhelmed by visual information?; Question 17. Have you ever noticed the presence of perceptual distortions when you have been tired or fatigued?; Question 25. Have you ever experienced a spread of tiny white / black dots resembling the 'static' of a badly-tuned television superimposed across your visual field?; and Question 29. Have you ever experienced transient illusory 'spider-web' type patterns superimposed on the visual world?*), and therefore were removed from the final model. No items cross-loaded onto different factors. All three factors contained at least 6 loadings, which is regarded as stable.

Eleven-items loaded onto Factor 1, which primarily reflected visual irritation or discomfort across a host of circumstances. Ten out of the eleven items (90%) overlapped with the Factor - *"Heightened Visual Sensitivity and Discomfort"* in the original *CHi* (see Braithwaite et al., 2015a) and so this title was retained as the title of this factor in the present case. Factor 2 items were primarily "*Aura-Like Visual Hallucinatory Experience*" which included 9 items that were related to visual aura-like experiences such as phosphenes, flashes of colour and other elementary visual hallucinations (including partial loss of visual information / scotomas). These items overlapped with both the factor *"negative aura-type visual aberrations"* and '*positive aura-type visual aberrations' from the* original *CHi.* Factor 3 contained 6 items related primarily to "*distorted visual perception*".

Table 3. The factor structure of the *CHi-II*

	Factor			Communalities	
	1	2	3	Initial	Extraction
4) Irritation from indoor lights?	**.785**	-.059	-.149	.514	.481
11) Felt dizzy / nauseous due to strong light or patterns?	**.723**	.076	-.145	.481	.488
13) Experienced visual discomfort from certain patterns?	**.687**	.020	-.074	.467	.438
18) Fluorescent lights irritate your eyes?	**.685**	-.071	-.020	.444	.408
16) Working on computer for long periods irritates eyes?	**.627**	-.106	.040	.425	.355
12) Lights or colours seem brighter or more intense?	**.619**	-.128	.136	.466	.397
14) Had a headache / migraine induced by visual information?	**.585**	.220	-.208	.431	.395
7) Find certain environments irritating?	**.534**	.033	.116	.485	.388
20) Headlights from oncoming traffic irritate eyes?	**.457**	-.025	.035	.302	.214
1) Vision more sensitive to external sensory information?	**.431**	.076	.223	.494	.396
21) Experienced visual discomfort from reading?	**.421**	-.114	.184	.356	.227
23) Experienced flashes of moving patterns?	.046	**.589**	-.053	.409	.342
24) Experienced loss of visual information?	-.001	**.563**	-.073	.356	.273
9) Ever experienced flashes of colour?	.016	**.544**	-.014	.412	.297
8) Ever seen fleeting shapes?	-.005	**.540**	.112	.415	.372
27) Ever had loss of vision surrounded by zigzag patterns?	-.128	**.501**	-.025	.373	.186
26) Ever seen coloured shapes, balls or patterns?	.001	**.466**	-.029	.300	.203
6) Ever experienced transient flashes or spots of white light?	.263	**.435**	.031	.456	.409
28) Ever experienced spiral, tunnel or funnel-like shape?	-.160	**.434**	.129	.317	.199
22) Experienced a narrowing of your visual field?	-.051	**.411**	.259	.334	.328
19) Had an out-of-body experience?	-.339	.105	**.629**	.305	.339
30) Experienced the world draining in colour and vibrancy?	.008	-.131	**.606**	.264	.295
3) Visual perception seems heightened or enhanced?	.271	-.116	**.476**	.435	.348
10) Find the appearance of things or people changes?	.062	.050	**.448**	.316	.266
5) Everyday objects look different?	.108	.022	**.415**	.325	.244
15) Experienced visual distortions when you look around?	.227	.013	**.412**	.403	.327
2) Overwhelmed by visual information?	.359	.108	.234	.489	.354
17) Noticed perceptual distortions when you are fatigued?	.341	.219	.144	.440	.355
25) Ever seen white/black dots across your visual field?	.154	.108	.199	.225	.151
29) Ever experienced 'spider-web' patterns?	.058	.329	-.096	.238	.099

Note: Item loadings for each factor (> .40) are listed in decreasing magnitude order (In **BOLD**). The shaded items are not loaded into any factors.

3.1.6 Reliability of the factor model

The correlations between the factors are summarized in Table 4. Similar to *CHi*, all the correlations between the factors were greater than 0.50, which suggests that there were more than 25% common variance between the factors. The significant correlations between the factors further justified the usage of oblique rotation methods in our EFA.

One hundred and ninety-eight subjects participated in T2 for the *CHi-II* questionnaire revisit. The average period between T1 and T2 was 16.8 days. The test-retest reliability coefficient of the total *CHi-II* scores between T1 and T2 was .81, suggesting a good stability for the *CHi-II* questionnaire as a trait scale. None of the inter-items correlations exceeded 0.7, suggesting no items should be removed due to redundancy (Boyle, 1992). The Cronbach's alpha of *CHi-II* was high at 0.90 (see Table 5). The first two factors both had an acceptable alpha (>.70) while the internal consistency of factor 3 was slightly lower (0.65 – 0.70).

Table 4. The correlation matrix between each of the extracted factors.

Factor	1	2	3
1			
2	.55		
3	.52	.59	

Table 5. The Cronbach's alpha for the *CHi-II* scale and the 3 factors

	CHi-II (full scale)	Factor		
		1	2	3
Cronbach's alpha	.90	.86	.76	.67

3.2 Results of Study 2

To complement the frequentist approach of Study 2, we have conducted Bayesian analyses using analytical software - JASP version 0.7.5.6, with the Cauchy prior width set as

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the default value 0.707 (Love et al., 2015; Rouder, Morey, Speckman, & Province, 2012).

The analysis estimates a Bayes Factor (BF_{10}) to make a comparison on the likelihood of

whether the data are more in favour of the alternative hypothesis ($BF_{10} > 1.0$) or the null-

hypothesis ($BF_{10} < 1.0$). For example, a BF_{10} of 10 suggests that the data fit 10 times better

with the alternative hypothesis than the null hypothesis. In contrast, a BF_{10} of 0.10 suggests

that the data fit 10 times better with the null rather than the alternative hypothesis (Jarosz &

Wiley, 2014). According to Jarosz and Wiley (2014), a BF_{10} of 3 – 10 can be interpreted as

moderate evidence in favour of the alternative hypothesis, 10 – 100 can be considered strong,

and > 100 considered very strong and decisive.

In line with previous recommendations, the LF grating was used as baseline stimuli in

the sense that the responses to this grating are used to screen for response bias and therefore,

were not formally analysed. The 95th percentile of the AVD score for LF grating was 18.3

with a 95% confidence interval (CI) of 15.7 – 21.7. Participants who scored higher than the

upper limit of the CI were discarded from the sample. Based on these criteria, 11 subjects

were removed from the sample, which gave a final sample size of 343. There were no clicks

on 'spacebar' and no lateralized responses of AVDs – so these factors were not analysed

further. To establish a baseline-corrected measure of pattern-glare, the AVD scores for the

HF baseline grating were subtracted from the AVD scores for the MF grating – ΔAVD (MF -

HF; see Wilkins & Evans, 2001; Evans & Stevenson, 2008).

3.2.1 The PG effect for the Control group

Among the sample, 316 participants were defined as non-migraineurs. We inspected the

distribution of the AVDs for each spatial frequency and these are summarised in Table 6.

Based on the current version of PG task, the upper limit of the normal range for ΔAVD was

determined by the 95th percentile, and it was 10.5 (95% CI: 8.7 – 14.8; see Table 6).

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Table 6. Descriptive statistics for the AVD score of the PG task for the control group.

	LF (0.5 cpd)	MF (3 cpd)	HF (15 cpd)	MF – HF (3 – 15 cpd)
Mean	4.53	12.6	11.6	1.00
Range	0 – 21.33	0 – 74.7	0 – 64.3	-19 - 26
Percentiles				
5	0	1.95	1.33	-8.00
25	1.00	5.33	4.67	-2.00
50	2.67	9.67	8.67	0.67
75	6.58	16.6	15.3	3.92
95	14.8	32.2	31.8	10.5

The sample was split in two groups at the 75th percentile of the ΔAVD. Subjects with a ΔAVD higher than 3.92 were classified into the high PG group while subjects with a ΔAVD lower than 3.92 became the low PG group. A one-way multivariate analysis of variance (MANOVA) was conducted to examine the mean score differences of *CHi-II* and *CAPE* between the high PG group and low PG group. The result suggested a significant multivariate effect, F (2, 313) = 3.21, p = .042; Wilk's λ = .98, partial η^2 = .02. Six post-hoc one-way ANOVAs were then conducted to compare the mean differences of each subscale of the questionnaire individually between the two groups with the False Discovery Rate correction being applied to correct for multiple comparisons (Benjamini & Hochberg, 1995). This revealed a significant effect of group on Factor 2 of the *CHi-II*, supporting the idea that participants with a higher ΔAVD scored significantly higher on *the aura-like hallucinatory experiences* (*AHE*) of *CHi-II* than participants with a lower ΔAVD score. There were no significant effects on the other *CHi-II* factors. Interestingly, there were also no reliable effects in relation to any components of the *CAPE* measure (see Table 7).

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Table 7. The mean questionnaire scores (with the SE in parentheses) and the results of ANOVAs for PG group vs. non-PG group comparisons.

Questionnaire	PG group (n = 79)	Non-PG group (n = 237)	*p*-value	*FDR adjusted p-value*	*BF*$_{10}$
HVSD	41.4(2.56)	36.1(1.21)	.038	.114	1.09
AHE	13.5(1.22)	9.77(0.67)	.007	.042	4.66
DVP	7.85(0.92)	6.56(0.46)	.181	.236	0.33
POS	13.6(0.90)	12.2(0.58)	.232	.236	0.28
DEP	15.8(0.87)	14.6(0.50)	.236	.236	0.28
NEG	21.2(1.22)	19.4(0.71)	.203	.236	0.31

Note: *CHi-II (1)HVSD: Heighted Visual Sensitivity and Discomfort; (2)AHE: Aura-Like Hallucinatory Experiences; (3)DVP: Distorted Visual Perception; CAPE: (1)POS: positive symptoms; (2)DEP: depressive symptoms; (3)NEG: negative symptoms*

3.2.2 The PG effect of migraineurs vs. non-migraineurs

To compare the pattern glare effect between migraineurs and non-migraineurs, a one-way between-subject ANOVA was conducted on ΔAVD. The results showed that the migraineurs group had a significantly higher ΔAVD, F = (1, 341) = 5.75, p = .017, *BF*$_{10}$ = 2.23 (see Figure 4). In addition, such group differences were not observed on the AVD score of both the low frequency and high frequency baseline gratings (both F < 0.1).
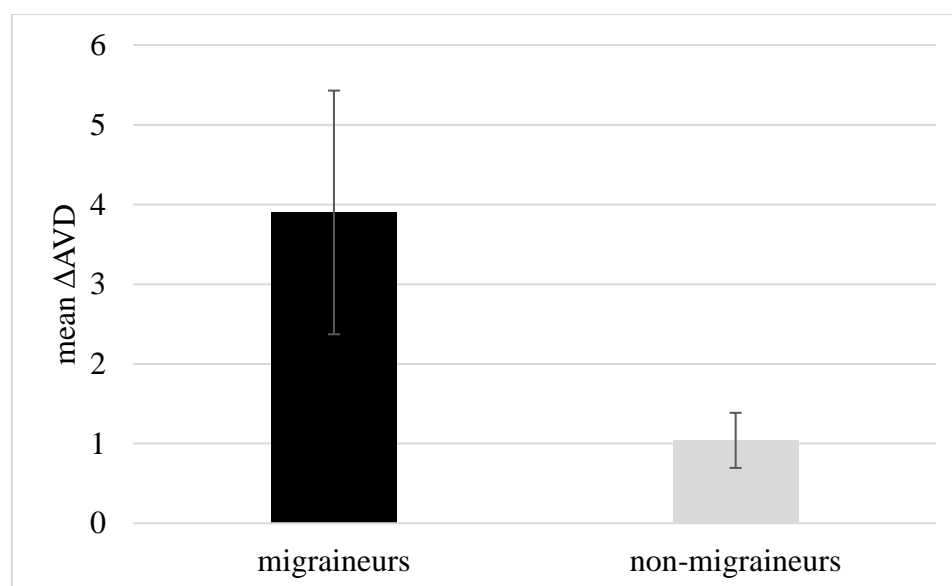

Figure 4. The difference in mean ΔAVD (AVD scores for MF subtracted by AVD scores for HF) between migraineurs and non-migraineurs. Error bars = +/- 1 S.E.

A MANOVA was used to compare the *CHi-II* and *CAPE* scores between migraineurs

and non-migraineurs. The result suggested that there was a statistically significant difference

in the questionnaire scores, F (2, 340) = 6.13, p = .002; Wilk's λ = .97, partial η^2 = .035. Post-

hoc tests showed that migraineurs scored significantly higher for *AHE*, F (1, 341) = 9.194, p

= .003, BF_{10} = 12.6 and *HVSD*, F (1, 341) = 8.259, p = .004, BF_{10} = 8.31 respectively (see

Table 8). In contrast, there were no significant group differences in *DVP*, or any components

of the *CAPE* measure.

Table 8. The mean questionnaire scores (with the SE in parentheses) and the results of
ANOVAs for migraineurs vs. non-migraineurs comparisons.

Questionnaire score	Migraineurs (n = 27)	Non-migraineurs (n = 316)	*p*-value	*FDR* adjusted p-value	BF_{10}
HVSD	49.9(5.23)	37.4(1.12)	.003	.012	12.6
AHE	16.9(2.57)	10.6(0.59)	.004	.012	8.31
DVP	5.89(1.00)	6.88(0.42)	.494	.741	0.26
POS	9.78(1.40)	12.6(0.49)	.107	.214	0.67
DEP	14.6(1.52)	14.9(0.43)	.823	.823	0.22
NEG	20.6(2.38)	19.8(0.61)	.741	.823	0.22

Note: *CHi-II* (1)*HVSD: Heighted Visual Sensitivity and Discomfort;* (2)*AHE: Aura-Like Hallucinatory Experiences;* (3)*DVP: Distorted Visual Perception; CAPE:* (1)*POS: positive symptoms;* (2)*DEP: depressive symptoms;* (3)*NEG: negative symptoms*

4. General Discussion

The present study examined distinct forms of anomalous experience and the

underlying role of both trait-based and state-based signs of cortical hyperexcitability in both a

self-declared migraine and non-neurological group. Several new findings were revealed.

Study 1 examined a revised and improved indirect proxy measure of cortical

hyperexcitability by exploring experiences thought to reflect underlying hyperexcitability

across a variety of conditions and disorders. Alongside Study 2, the present investigation was

methodologically improved in a number of important ways, which included the recruitment

of a larger sample, an examination of test-retest reliability, and a more intuitive loading of

items onto factors.

The revised and improved *CHi-II* produced a 3-factor model obtained from the

exploratory factor analysis in Study 1. The EFA revealed separate and distinct loadings for

different phenomenological aspects relating to visual aberrant experiences. Each factor is

now discussed.

4.1 The factor structure of *CHi-II*

Factor 1 - *Heightened Visual Sensitivity and Discomfort (HVSD)*

Ten out of the eleven items of this factor overlapped with the largest factor from the original

CHi (Braithwaite et al., 2015a). This factor explained the largest amount of common variance

with the highest eigenvalues among the extracted factors. The experiences that loaded onto

this factor appear to be related to excessive light / pattern induced sensitivity and discomfort.

Interestingly, there were no perceptual distortions at all on this factor. In addition, the

Cronbach's alpha (> .80) suggested that the responses to these items were highly consistent

with each other – an observation further bolstered by the near perfect replication of the

original study for this factor. Pattern and light induced visual stress symptoms (which can

include induced somatic discomforts) are consistent with the notion of elevated

hyperexcitability in visual cortex and have been well documented in studies on migraine and

non-clinical samples predisposed to aberrant perceptions and hallucinations (Braithwaite et

al., 2013; Braithwaite, Mevorach, & Takahashi., 2015; Harle, Shepherd, & Evans, 2006;

Huang et al., 2003; Wilkins, 1995).

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Factor 2 – *Aura-Like Hallucinatory Experiences (AHE)*

This factor consisted of 9 items that related primarily to hallucinatory visual experiences, either describing low-level elementary hallucinations (phosphenes, flashes, colours, patterns and spots) or loss of visual information (scotoma, tunnel vision, blurred vision, visual field defects or complete blindness), and therefore, was named here as *"aura-like hallucinatory experience"*. Three items could be regarded as scotoma, describing 3 different ways of diminshed visions, and therefore were considered as negative aura. Six items could be considered as positive aura experiences since they were low level elementary visual hallucinations superimposed onto the visual world . Unlike the original study, both positive and negative aura-like experiences converged to form one single and stable factor which is arguably a more parsimonious solution relative to the orginal *CHi* measure. The superior sample size and good reliability / consistency in the present study would suggest that the present factor structure is improved relative to the original study.

Factor 3 – *Distorted Visual Perception (DVP)*

This "*Distorted Visual Perception"* factor contained 6 items, associated primarily with visual distortions. Five items can be classfied as visual distortions since they described changes of visual perceptions (e.g. distortions in color, shapes, etc) to people, objects, or the physical environment. The only exception to this was the item on out-of-body experiences (OBEs), which also loaded onto this factor and is conceptualised as a higher-level and complex hallucination resulting from a breakdown in multisensory integration (Blanke & Arzy, 2005; Blanke et al., 2005; Blanke, Landis, Spinelli, & Seeck, 2004; Braithwaite & Dent, 2011). It was also the strongest loading item on this factor. The explanation for this is not entirely obvious or clear. It is noteworthy that although the OBE item may sound qualitatively different to the other items on this factor, body image distortions and indeed OBEs have been

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previously reported by migraine patients (a condition associated with cortically mediated hyperexcitability: Ilik & Ilik, 2014; Morrison, 1990).

One possibility might be that the notion of 'distortions' can also be extended to body-experiences (distortions in introception) as well as perceptions of the outside world (extroception). For example, the OBE is reliant on both a failure of multisensory integration and a hallucinatory mental model of the self in space and time (Blanke & Mohr, 2005; Braithwaite & Dent, 2011). One admittedly speculatory possibility is that the former process can be viewed more as a *distortion* in body perception and the latter as an additional hallucinatory component. Therefore it might be the case that the association between this question and the notion of distorted perception pertains to the first part of this complex process and not the latter (though both are correlated). Unfortunately the current *CHi-II* measure did not utilise any additional questions on body-distortion experiences to explore the utility of such speculations.

There were 4 items (Q2, Q17, Q25, Q29) failing to load onto any of the above factors. As a result, 26 items survived in the final EFA model. Interestingly, these 3 common factors all contained an intuititive descripter that summarized the characterisitics of the loaded items consistently and coherently (see Figure 5).
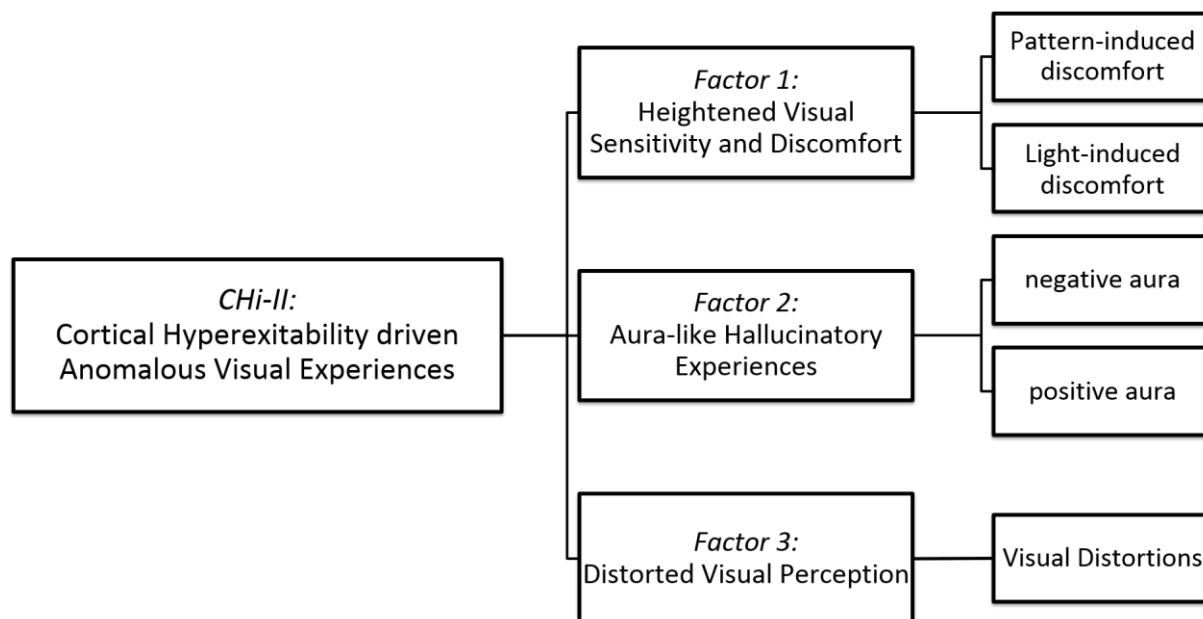
Figure 5. A summary of the 3-factor structure of the *CHi-II.*

These 3 significantly separable factors, revealed by the EFA and the PA, suggest several dimensions underlying different thematic types of anomalous experience. This is consistent with the notion that not all forms of experience may necessarily reflect the same processes or networks. This observation significantly extends previous research, which has generally clumped all forms of aberrant experience into one unitary notion of cortical hyperexcitability, visual stress, or photophobia (Aurora et al., 1999; Aurora & Wilkinson, 2007; Conlon et al., 1999; Wilkins, 1995). Also, the item-loadings of the *CHi-II* appear to be more intuitive than that reported previously – suggesting an improved utility as an indirect proxy measure.

4.2. The relationship between the CHi-II factors and PG task results

The utility of this model was examined further in Study 2 via comparison to a computer-based pattern-glare assessment of cortical hyperexcitability and extended further still with a self-reported migraine group. Within the control group, people who reported a stronger PG effect also scored higher on the *aura-like hallucinatory experiences* (*AHE*; $p = 0.007$, $BF_{10} = 4.66$) factor, relative to those reporting weaker PG effects. This supports the hypothesis that there is a relationship between state-based PG effects and the presence of trait-based aura-like experiences represented on this factor (i.e., phosphenes, flashes, colours, scotomas, tunnel vision, etc.). However, the association with the PG effect was not reliable, after correction for multiple comparisons, for the *heightened visual sensitivity and discomfort* (*HVSD; p = .*114, $BF_{10} = 1.09$) factor and was completely unobservable for the *distorted visual perception* (*DVP*; $p = .236$, $BF_{10} = 0.33$).

In addition, the present findings support the notion that migraineurs generally have a more hyperexcitable visual cortex compared to the control group with a higher PG effect ($p = .017$, $BF_{10} = 2.23$). As expected and being consistent with previous migraine research, the migraine group was significantly more susceptible to aura-like hallucinations and visual stress symptoms relative to the non-migraine control group by scoring higher in the *AHE factor* ($p = 0.004$, $BF_{10} = 8.31$) and the *HVSD* factor ($p = 0.003$, $BF_{10} = 12.6$). As with the control group, those reporting migraines did not appear to score significantly higher on the *DVP* factor than controls.

One common issue in research on hallucinations / aberrant perceptions is the extent to which the findings can be accounted for in terms of a generic underlying response bias.

Hallucinating participants can be predisposed to such biases (Deviant Response pattern; Berg, 1955, 1959; Berg & Collier, 1953); however, there are a host of reasons why this view is unlikely to be a tenable counter-explanation for the present findings.

For example, although generic response biases have indeed been documented in hallucinating groups, this association is related more to those with such experiences occurring with psychosis and schizophrenia – and thus not necessarily a group predisposed to anomalous perceptions per-se (Adams & Berg, 1961; Berg, 1955; Cowen, Staiman, & Wolitzky, 1961; Peters et al., 2013; Sechrest & Jackson, 1963). In addition, the observation of clear, separable and intuitive factors for the *CHi-II* measure is not tractable to the notion of a generic underlying response bias, which should influence the endorsement of all items roughly equally. Clearly, this did not happen.

Furthermore, participants scoring high on responses to the low-frequency grating of the pattern-glare task (taken as an index of a generic response bias) were removed from the sample (Study 2). Finally, it is noteworthy that none of the factors from the *CAPE* measure were significantly related to PG scores – providing direct evidence here that any predisposition to aberrant beliefs (intuitions, thoughts, feelings, reasoning etc.) was not associated to predisposition to report aberrant perceptions elicited by the presentation of aversive visual gratings. Put simply, the PG effects observed here did not appear to reflect predisposition to endorse questions erroneously. Collectively, the findings reported in the present study do not appear to be mediated by aberrant belief processes or generic response biases commonly seen in broader research on hallucinations occurring in psychosis and schizophrenia.

4.3 Theoretical Implications

The existence of the three-factor model suggests multiple contributions to the general concept of cortical hyperexcitability. This fractionation provides researchers with new and refined precision in delineating these underlying features – not all of which may actually reflect hyperexcitability at the cortical level.

The results of *AHE* indicate that a hyperexcitable visual cortex is more susceptible to elementary hallucinations (both of a positive and negative nature: see also Aurora & Wilkinson, 2007; Boulloche et al., 2010; Chen et al., 2011; Denuelle et al., 2011; Huang et al., 2003; Wilkins, 1995; Wilkins et al., 2004). According to the cortical spreading depression (CSD) model for migraine, CSD is more likely to occur in, and propagate over, a hyperexcitable cortex, including primary and extrastriate visual cortex, generating positive aura (associated with a precipitating depolarization) or negative aura (associated with a subsequent hyperpolarization) symptoms such as fortification, phosphenes, colours, and scotomas (Bowyer et al., 2001; Braithwaite et al., 2015a; Hadjikhani et al., 2001; VanValkenburgh, 2005).

Although CSD is thought to originate in visual cortex, it is not the only region responsible for mediating aura experiences. Multiple cortical regions beyond the visual area can be activated throughout a migraine attack with distinct implications for reported phenomenology (Bowyer et al., 2001; Cao et al., 1999; Cao, Aurora, Nagesh, Patel, & Welch, 2002; Dahlem, Engelmann, Lowel, & Muller, 2000; Dahlem & Hadjikhani, 2009; Hadjikhani et al., 2001; Lauritzen, 2001; Welch, Cao, Aurora, Wiggins, & Vikingstad, 1998; Zhang et al., 2010). For example, several researchers have proposed that the trigeminovascular system could be modulated by the visual cortex amongst other associated neural structures such as somatosensory insular cortex and the subcortical region (e.g. hypothalamus and brainstem), causing painful migraine headaches and photophobia symptoms (see Noseda et al., 2011; Noseda & Burstein, 2013).

In addition, if CSD depolarizes the cortical regions that process vestibular signals (e.g. posterior insula and temporoparietal junctions), symptoms such as vertigo, dizziness, nausea and motion sickness could be formed (Cutrer & Baloh, 1992; Lempert, Neuhauser, & Daroff, 2009). Collectively, the excitability of any structures within the cortico-subcortical-trigeminovascular networks could possibly make an impact on *HVSD* symptoms. This might help to explain why the PG effect was strongly associated with the *AHE* in both populations but only associated with responses on the *HVSD* for the migraine group – as only this group may have also experienced pain-related symptoms along with visual symptoms.

The failure of the *DVP* factor to be associated with PG scores for both migraineurs and high-PG scoring control participants might suggest that *DVP* related experiences do not reflect aberrations in cortical areas or processes responsible for mediating the responses evoked by aversive patterns. Although *DVP* factor is positively correlated with *AHE* and *HVSD* , and occur as migraine aura symptoms, they are far less common compared to these two factors (Russell & Olesen, 1996). Statistically speaking, the eigenvalue and internal consistency of the *DVP* factor was the lowest amongst the 3 factors, which means that there were larger amounts of unexplained variances and the items are less likely to covariate with each other. Taken all this into account, it is possible that the *DVP* score may be driven by an even wider range of abnormal neural activities than the other two factors which may indeed reflect a truer representation of what has commonly become known as cortical hyperexcitability. Such possibilities remain speculative at the present time but represent an exciting premise and avenue for future research.

It is particularly noteworthy that we found the high susceptibility to visual aura-like symptoms is not limited to migraine patients, but also observed amongst non-migraine populations. In line with previous studies, our findings support the idea that healthy participants might also show signs of aberrant neural responses and anomalous experiences –

similar to that seen (albeit in attenuated form) for the migraine group. This is also consistent with the theory of a continuum of predisposition to anomalous visual experiences and hallucinations (McCreery & Claridge, 2002; Langer, Cangas, & Gallego, 2010; Schwartzman, Maravic, Kranczioch, & Barnes, 2008). What is even more noteworthy is that our present findings show this effect for non-neurological groups and restricted primarily to aberrant perceptions not aberrant beliefs – providing increased precision on the nature of the anomalous perceptions possible in such groups.

4.4 Potential Limitations & Future Research

The *CHi-II* is based on previous research from earlier measures and established research from the cognitive neurosciences. However, it should be acknowledged that questionnaire measures are not, in and of themselves, a direct instrument for quantifying underlying neural processes – more the sorts of experiences associated with aberrant neural processes. Perhaps the most useful and helpful way to view and utilise such tools is as an indirect 'proxy' measure indicative of aberrant neural processes that can reflect hyperexcitability – or is known to in the broader literature.

Nonetheless, the items making up the *CHi-II* have been associated with increased levels of cortical activation revealed by more direct measures from the cognitive neurosciences which include neuroimaging, neurophysiology and behavioural studies (Adjamian et al., 2004; Aurora, Ahmad, Welch, Bhardhwaj, & Ramadan, 1998; Boulloche et al., 2010; Chouinard, Zhou, Hrybouski, Kim, & Cummine, 2012; Coutts et al., 2012; Dahlem & Chronicle, 2004; Datta et al., 2013; Huang et al., 2003; Huang et al., 2011; Martín et al., 2011; Welch et al., 2001). Furthermore, the selective role for the different factors in relation to the level of pattern-glare reported is revealing and suggests some specificity in the thematic nature of the experiences reported.

Another possible argument might be that the inter-correlations among the items were caused by their semantic overlaps rather than driven by the associated underlying neurological/ mechanisms. First, the internal consistency and inter-correlations of the items did not suggest redundancy of any items. Second, most of the items listed in *CHi-II* were semantically specific to describe some cortical hyperexcitability related symptoms. These items were documented as experienced by patient groups such as migraine with aura and Meares-Irlen syndrome who are known to have increased level of cortical excitability. Importantly, the second part of this study showed that the latent factors were associated with the visual discomforts and distortions caused by the gratings. Therefore, both intuitively and statistically speaking, the *CHi-II* is a behaviourally based rather than semantically based trait scale.

Alongside internal consistency and test-retest, external validity is another critical element which needs to be addressed in promoting the efficacy of any new measurement, including *CHi-II*. It has been argued that external validity of measures is superior with fewer factors in the structure, more accurate reflections on theoretical constructs, and supportive findings that will repeat under identical conditions (Lucas, 2003; Henson & Roberts, 2006). In our Study 1, we have retained only the three most stable factors from *CHi-II* in the factor structure, which was further verified / validated by an independent sample reported in our second study (Study 2), where migraineurs scored high on two of the factors. These findings, together with the extensive reports of using PAF, the number of extracted factors, and rotation method in our study which allows the model to be evaluated externally by new sample data, demonstrated a modest external validity of *CHi-II*.

One thing we cannot completely rule out is the possibility that there are other underlying factors co-existing with cortical hyperexcitability to drive the latent structure and the association between the scales and the PG task. For example, the *HVSD* scale and the

visual discomfort response in PG task could be mediated by perception and tolerance of pain.

Therefore, we can expect the existence of diverse brain regions (including but not limited to

insula, somatosensory cortex, thalamus, cerebellum and brainstem) that are engaged in the

processing of visually induced pain and headache (Bahra, Matharu, Buchel, Frackowiak, &

Goadsby, 2001; Coppola et al., 2010, 2018; Vincent & Hadjikhani, 2007). Further research

using the *HVSD* and *AHE* factor as covariates of more objective measurements (e.g. brain-

imaging or electroencephalography) to reflect the actual aberrant neurophysiological activity

of the visual cortex might prove insightful in this regard. Not only would it help confirm the

factor structure but also the *CHi-II* itself can complement those experimental protocols by

providing a formally established behavioural construct to connect aberrant visual perceptions

and the underlying brain activities together.

The migraine group was not particularly large, was based on self-reports and there

was no direct medical screening or finer-grained delineation of the many migraine / headache

sub-types. Consequently, our findings here should be viewed as tentative with regards these

complex concepts. Building on the current findings, future research would benefit from a

more comprehensive and fine-grained analysis of the migraine condition, and its sub-

divisions, in relation to the separate *CHi-II* factors and the PG task. Although the current

sample was not sufficient to explore these factors in full, it was sufficient to establish the

scientific premise that our self-declared migraineurs did indeed display signs of significantly

increased levels of PG experiences, arguably reflecting aberrant levels of cortical

hyperexcitability. This observation was further extended here in that migraineurs displayed

distinct ratings exclusively to the *AHE* and *HVSD* factors – a degree of specificity not

previously observed and not easily explained by notions that the migraine group here might

reflect a vastly more heterogeneous group than is useful for theory.

The utility of the *CHi-II* can be further examined via coupling its use to more objective methods such as brain stimulation (magnetic and electric) and neuroimaging (Aurora et al., 1998; Antal, Kriener, Lang, Boros, & Paulus, 2011; Huang et al., 2003; Kanai, Paulus, & Walsh, 2010). Indeed a recent study demonstrated, for the first time, that pattern-glare effects could be increased via anodal stimulation montages using transcranial direct current stimulation (tDCS), but more so for those who already displayed a lability for cortical hyperexcitability (Braithwaite et al., 2016). It would also be prudent to determine how the separate factors from the *CHi-II* dovetail with different neurological, psychiatric, and clinical disorders. As with the migraine group reported in the present findings, hyperexcitable groups may only score high on some factors and not others, with such patterns providing informative covariates in a broader assessment of aberrant neural processes and resultant anomalous experience. In conclusion, we propose that the *CHi-II* is a robust, improved and comprehensive indirect proxy measure of aberrant perceptions and some factors appear to be associated with cortical hyperexcitability. Its factor structure and the novel findings reported here enables future researchers to investigate the weighted contribution of these factors to different types of visual symptoms across a host of conditions and disorders, suggesting that it could have considerable scientific and clinical utility.

Cortical Hyperexcitability

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