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ORIGINAL PAPER

# Visual-stress-related cortical excitability as a prospective marker for symptoms of depression and anxiety in young people

**Christy Lai-Ming Hui[1] · Stephanie Ming-Yin Wong[1] · Terrence Yat-To Yu[1] · Terry Tak-Yee Lau[1] · Olivia Choi[1] · Samantha Tsang[1] · Yi-Nam Suen[1] · Bess Yin-Hung Lam[1] · Corine Sau-Man Wong[1] · Simon Sai-Yu Lui[1] · Kai-Tai Chan[1] · Michael Tak-Hing Wong[1] · Gloria Hoi-Yan Wong[2] · Sherry Kit-Wa Chan[1,3] · Edwin Ho-Ming Lee[1] · Wing-Chung Chang[1,3] · Arnold Wilkins[4] · Eric Yu-Hai Chen[1,3]**

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## Abstract

Visual stress is thought to reflect cortical excitability and has been associated with many neurological, neuropsychiatric, and neurodevelopmental conditions. However, its relationships with symptoms of depression and anxiety have not yet been elucidated. We conducted two separate studies to first examine visual stress in a longitudinal community sample of 104 participants (aged 12–24) in association with prospective symptoms of depression, anxiety, and distress after 3 months, and subsequently in a cross-sectional epidemiological sample of 530 participants (aged 15–24) to validate its associations with current mood and distress symptoms. The Pattern Glare Test was used to examine visual stress to three grating patterns with the spatial frequencies (SF) of 0.3, 2.3, and 9.4 cycles per degree (cpd). Other known factors of mental health, including functioning, as well as resilience, hopelessness, and loneliness, were also assessed at baseline. In both studies, we showed that perceptual distortions were highest toward the pattern with mid-SF (2.3 cpd). Multiple linear regression analyses revealed that greater visual stress was significantly associated with not only baseline but also 3-month symptom outcomes, even when accounting for age, years of education, days of no functioning, resilience, hopelessness, and loneliness. Our findings suggest the importance of visual stress in understanding and predicting poor mental health outcomes. As mental health can lead to far-reaching consequences that extend to adulthood, our findings may inform state-of-the-art innovative strategies for the prediction of poor mental health outcomes and suggest visual stress as a potential marker for early risk detection among young people.

**Keywords** Mental health · Pattern glare · Perceptual distortions · Youth

## Introduction

First coined by Wilkins et al. [1], visual stress refers to a susceptibility to visual discomfort and perceptual distortions when viewing certain visual patterns, especially strong stimuli such as striped patterns with high-contrast energy at a mid-spatial frequency (SF) of 3 cycles per degree (cpd). The degree to which these are experienced depends on the visual characteristics of the pattern (e.g., spatial frequency) and shows considerable variation from one individual to another. Susceptibility to visual stress is typically evaluated using the Pattern Glare Test, a simple measure of visual discomfort in response to striped patterns ranging from low to high SF: Pattern 1 (0.3 cpd), Pattern 2 (2.3 cpd), and Pattern 3 (9.4 cpd) at the viewing distance of 40 cm [1, 2]. Of note, Pattern 2 is among the only pattern with high-contrast

Stephanie Ming-Yin Wong: co-first author.

✉ Eric Yu-Hai Chen
ericchen.hku@gmail.com

1 Department of Psychiatry, School of Clinical Medicine, Faculty of Medicine, Li Ka Shing, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong SAR, China

2 Department of Social Work and Social Administration, The University of Hong Kong, Hong Kong, China

3 State Key Laboratory of Brain and Cognitive Sciences, University of Hong Kong, Hong Kong, China

4 Department of Psychology, University of Essex, Essex, UK

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gratings at mid-SF, which is expected to trigger maximum pattern glare [2, 3]. Meanwhile, Patterns 1 and 3 (with gratings at lower and higher SFs, respectively) were included as control stimuli and are expected to elicit fewer perceptual distortions [3]. Visual stress has been found to be associated with a range of neurodevelopmental disorders, including epilepsy, dyslexia, autism, head injury, and migraines [4]. Furthermore, high levels of visual stress have been linked to increased brain activity in the visual cortex [5].

The predominant hypothesis of visual stress indicates a cortical mechanism involving visual cortical hyper-excitability that is related to imbalances in neural systems [6]. Specifically, inhibitory neurotransmitters (e.g., gamma-aminobutyric acid, GABA) may fail to sufficiently regulate high levels of stimulation in the excitatory system resulting from strong visual stimuli. Indeed, fMRI studies have demonstrated an association between visual stress and bilateral brain activation in the visual cortex [5]. Perceptual distortions have also been reported at higher rates among participants whose visual cortex was more excitable in a study comparing cortical excitability of patients with migraine with aura and those without aura [7]. Impairments in the GABAergic inhibitory system may therefore enable gratings with mid-SF to provoke visual perceptual distortions and discomfort, as neurons fire inappropriately.

The neural maturation of the excitatory and inhibitory systems occurs between late childhood and adolescence—the same period during which mental health systems and disorders typically emerge. Indeed, abnormality in the GABA system has been implicated in mood disorders such as depression and anxiety. For instance, the ratio of inhibitory–excitatory transmitters in the occipital cortex differs in major depressive disorders (MDD), such that they were observed to be at lower and higher concentrations, respectively, than healthy controls [8]. Likewise, generalized anxiety disorder (GAD) has been hypothesized to involve a deficiency in either receptor sensitivity or in inhibitory neurotransmitters of the GABA system. Facilitating GABA activity through drug-induced methods (e.g., benzodiazepines) has shown to be effective in the treatment of GAD [9]. Considering the contributions of GABA, there is a potential for visual stress to be relevant to the mental health conditions of young people.

Relative to neurodevelopmental disorders, however, there is little research regarding the relationship between visual stress and common mental health disorders. One of the few studies in this area compared 24 Chinese patients with MDD and 30 healthy controls [10]. Using the Pattern Glare Test, MDD patients were found to show significantly higher visual discomfort and produced the most glare specifically for patterns with mid-SF (2.3 cpd) than controls. As expected, no significant difference was observed between the groups for the other two patterns. The authors postulated that the reduction in GABA neurotransmitters typically found in MDD patients may have contributed to greater deficits in cortical inhibition, thereby producing more pattern glare. Nonetheless, the novel finding that visual stress may contain a signal predicting mental health states requires careful characterization and replication. There is also a need to identify whether such findings can be extended to other common mental health issues as well, including GAD and psychological distress.

Given the importance of youth mental well-being, establishing a simple and reliable marker that indicates those at higher risk for poor mental health is crucial. We report findings from two separate studies to (1) first examine visual stress as a potential predictor of a range of symptom dimensions using a 3-month follow-up community sample of young people (Study 1), and (2) second validate the findings using a separate cross-sectional sample of young people from a representative household-based epidemiological youth sample (Study 2). We hypothesized that greater visual stress (particularly to 2.3 cpd) would be predictive of the severity of depressive and anxiety symptoms, as well as psychological distress, not only at baseline but also at 3 months.

## Study 1: longitudinal community youth sample

### Method

#### Participants

Between 23rd December 2019 and 18$^{th}$ March 2020, 104 young persons aged between 12 and 24 years were recruited in Hong Kong through an ongoing community-based project (LevelMind@JC) funded by the Hong Kong Jockey Club Charities Trust [11]. In collaboration with six local NGOs, the Department of Psychiatry at the University of Hong Kong is responsible for running this youth mental wellness project. The project aims to set up a series of community-based, youth-specific mental health hubs that involve youth workers and cross-disciplinary collaboration. Young people recruited in this study are receiving services provided by the Integrated Children and Youth Service Centers (ICYSCs) in Hong Kong. We included youths who were (1) aged 12–24 years, (2) had no impairment in corrected visual acuity, (3) were able to understand the nature of the study and (4) to give written informed consent and (5) were capable of communicating with the researcher. We excluded those who had (1) a known history of neurological disorders or seizures, (2) inadequate visual acuity with corrected vision, (3) implanted cardiac pacemakers or other electronic or metallic devices, (4) a history of head injury or brain surgery, or (5) alcohol or substance abuse in the recent 3 months.

Written informed consent was obtained from all participants or from their parents or legal guardians for those below the age of 18 years. Ethical approval was obtained from the Institutional Review Boards of the University of Hong Kong/Hospital Authority Hong Kong West Cluster and carried out in accordance with Good Clinical Practice and the Declaration of Helsinki.

### Study design and assessments

This was a prospective, 3-month follow-up study of 104 young people in Hong Kong. Data were systematically collected at baseline and after 3 months through a face-to-face interview by trained research assistants. Basic demographic information including age, gender, years of education, place of birth, and employment status were recorded. Visual stress and other possible predictors of mental health were also assessed at baseline, including personality and psychological constructs. Outcome measures of depressive and anxiety symptoms and distress were examined at 3 months.

### Pattern glare test

Participants were asked to complete a Pattern Glare Test with a trained research assistant to assess visual stress. The test was adopted from the original Pattern Glare Test [2], and consists of three patterns with different spatial frequencies. All patterns were printed on a white sheet of A4 paper and presented to the participant at arm's length. The three patterns were sequentially shown from Pattern 1 (0.3 cpd), to Pattern 2 (2.3 cpd), to Pattern 3 (9.4 cpd). For each pattern, participants were asked to fixate on the central point of the pattern for 5 s. After which, they were asked whether they could perceive any of the following 7 symptoms in the pattern: colors, listed as red, green, blue or yellow, the bending, blurring or shimmering of lines, any fading or shadowy shapes among the lines, or any other specific patterns. By summing the total number of "yes" responses, a pattern glare score was generated for each pattern. In addition to these seven symptoms for determining their composite pattern glare score, participants were asked if they suffered from any discomfort, nausea, dizziness, or unease to evaluate their levels of visual discomfort.

### Clinical outcomes

The primary outcome measures were mental health symptoms as assessed using the Patient Health Questionnaire—9 (PHQ-9; [14]), the Generalized Anxiety Disorder—7 (GAD-7; [15]), and the Kessler Psychological Distress Scale (K6; [16]).

The PHQ-9 is a 9-item self-administered screening tool for depression. The symptoms as described by the items align with the diagnostic criteria of MDD in the DSM-IV, and are scored on a 4-point Likert scale (0 = "Not at all" to 3 = "Nearly every day") based on their experienced frequency "over the past 2 weeks". To indicate severity, a total score is calculated by summing all items (range = 0–27), with a higher score indicating more severe depressive symptoms.

The GAD-7 is a 7-item self-administered screening tool for anxiety. The items align with the diagnostic criteria of GAD in the DSM-IV, and are scored on a 4-point Likert scale (0 = "Not at all" to 3 = "Nearly every day") according to the frequency at which the individual is bothered by the problem "over the past 2 weeks". The total score ranges from 0 to 21, with higher scores reflecting more severe anxiety symptoms; a score of above 10 is considered to fall into the clinical range.

The K6 is a 6-item self-report measure of psychological distress. Participants are asked to score on a 5-point Likert scale (0 = "None of the time" to 4 = "All of the time") with reference to the frequency of the given emotional states experienced "in the past 4 weeks". Some examples include "feel tired out for no good reason", "feel restless or fidgety", and "feel that everything was an effort". Scores on all items are summed to generate a total score (ranging from 0 to 24), with higher scores indicating higher levels of psychological distress.

### Basic demographics, personality, and psychological factors

Basic demographics collected included age, total years of education excluding kindergarten, gender, occupational status, place of birth, and any family psychiatric history. Other potential predictors of mental health symptoms that were assessed including (1) the total number of days of having no functioning due to emotional distress (with reference to items from the K6 [13]), the 10-item Connor–Davidson Resilience Scale (CD-RISC-10) [15], Beck Hopelessness Scale (BHS) [16], and UCLA Loneliness Scale [17].

### Statistical analysis

All analyses were carried out in IBM® SPSS® Version 25.0. The level of statistical significance for all analyses was set at $p < 0.05$. The relationships between pattern scores on the Pattern Glare Test and symptom outcomes were analyzed using Spearman's rank correlation. Due to the skewness in the distribution of pattern glare scores, comparisons between dichotomous groups were

conducted using Mann–Whitney *U* test. To account for other significant predictors in the relationship between pattern glare and mental health outcomes, a multiple linear regression analysis was performed for each of the three clinical outcomes (i.e., symptoms of depression, anxiety, and psychological distress). Pattern scores and significant correlates of symptom outcomes were included as the independent variables, while symptom outcomes were entered as the dependent variable. Out of the three pattern glare scores, only those on Pattern 2 were used; the high degree of correlation between the three scores would introduce collinearity if they were to be included in the same regression analysis.

**Table 1** Characteristics of the longitudinal community youth sample at baseline ($n = 104$)

| Characteristics | Frequency (%) |
|---|---|
| Background factors | |
| Age, mean (SD) | 18.2 (2.69) |
| Gender | |
| Male | 49 (47.1) |
| Female | 55 (52.9) |
| Education years, mean (SD) | 12.0 (2.31) |
| Occupational status | |
| Student | 80 (76.9) |
| Employed | 15 (14.4) |
| Unemployed | 9 (8.7) |
| Place of birth | |
| Hong Kong | 85 (81.7) |
| Mainland China | 19 (18.3) |
| Has family member(s) with psychiatric illness | 21 (20.2) |
| Functioning | |
| Days of no functioning in past 30 days due to emotional distress, mean (SD) | 1.2 (4.17) |
| Psychological factors | |
| Resilience (CD-RISC-10), mean (SD) | 23.9 (7.01) |
| Hopelessness (BHS), mean (SD) | 7.5 (3.64) |
| Loneliness (UCLA), mean (SD) | 44.6 (8.59) |

*BHS* beck hopelessness scale, *CD-RISC-10* 10-item Connor–Davidson Resilience Scale, *cpd* cycles per degree, *UCLA* UCLA Loneliness Scale

## Results

### Descriptive statistics on demographics and pattern glare

The demographic characteristics of the 104 young people at baseline from the longitudinal community sample were summarized (Table 1). The sample consisted of 47.1% male, with a mean age of 18.2 years and mean education (excluding kindergarten) of 12.0 years. Most of the participants were students (76.9%). While 18.3% of the population migrated from Mainland China, 81.7% were born locally in Hong Kong.

Pattern 1 was found to have significantly lower pattern scores than both Patterns 2 and 3 ($p < 0.001$) (Table 2).

### Predictors of mental health symptoms at 3 months in the longitudinal community youth sample

At 3 months, the mean and SD were $5.15 \pm 4.93$ for PHQ-9, $3.97 \pm 4.41$ for GAD-7, and $4.97 \pm 4.33$ for K6. These symptom profiles indicate that the sample consisted of youths with clinically diverse levels of emotional distress. For instance, PHQ-9 has a standard deviation of close to 5, which is large enough to account for a clinical difference [18].

To explore the relationships between baseline predictors and symptom outcomes at 3 months, a series of correlation analyses were performed (Table 3). Demographic information and significant univariate predictors, as appeared in any of the symptom outcome measures, were selected: age, total years of education, days of no functioning due to emotional distress, hopelessness, loneliness, and Pattern 2 scores.

### Associations between visual stress at baseline and mental health symptoms at 3 months in the longitudinal community youth sample

Multiple linear regression models were then conducted to examine the relationship between the potential predictors (i.e., Pattern 2 scores and other significant univariate predictors) and symptom outcomes at 3 months (i.e., PHQ-9,

**Table 2** Pattern glare scores of the longitudinal community youth sample at baseline ($n = 104$)

| Patterns | Mean (SD) | Statistical comparisons | |
|---|---|---|---|
| | | Pattern 1 vs. pattern 2 | Pattern 1 vs. pattern 3 |
| Pattern 1 (0.3 cpd) | 0.5 (0.79) | $z = 6.73$, $p < .001$*** | $z = 6.00$, $p < .001$*** |
| Pattern 2 (2.3 cpd) | 1.5 (1.20) | | |
| Pattern 3 (9.4 cpd) | 1.4 (1.33) | | |

*cpd* cycles per degree

*** $p < 0.001$

**Table 3** Univariate associations between potential predictors and outcome measures at 3-month follow-up in the longitudinal community youth sample ($n = 104$)

| Baseline predictors | Outcomes at 3 months | | | | | |
|---|---|---|---|---|---|---|
| | PHQ-9 | | GAD-7 | | K6 | |
| | $r_s$ | $p$ | $r_s$ | $p$ | $r_s$ | $p$ |
| Age | 0.22 | 0.022* | 0.27 | 0.006** | 0.28 | 0.005** |
| Total years of education | 0.16 | 0.107 | 0.18 | 0.075 | 0.21 | 0.030* |
| Days of no functioning in past 1 month due to emotional distress | 0.38 | < 0.001*** | 0.46 | < 0.001*** | 0.41 | < 0.001*** |
| Resilience (CD-RISC-10) | − 0.18 | 0.068 | − 0.12 | 0.217 | − 0.17 | 0.094 |
| Hopelessness (BHS) | 0.40 | < 0.001*** | 0.29 | 0.003** | 0.44 | < 0.001*** |
| Loneliness (UCLA) | 0.40 | < 0.001*** | 0.36 | < 0.001*** | 0.43 | < 0.001*** |
| Visual stress (pattern 2)[a] | 0.29 | 0.003** | 0.26 | 0.008** | 0.26 | 0.007** |
| | $U$ | $p$ | $U$ | $p$ | $U$ | $p$ |
| Gender | 1236.5 | 0.47 | 1089.5 | 0.090 | 1255.0 | 0.27 |

*BHS* Beck Hopelessness Scale, *CD-RISC-10* 10-item Connor–Davidson Resilience Scale, *UCLA* UCLA Loneliness Scale, *PHQ-9* Patient Health Questionnaire, *GAD-7* generalized anxiety disorder—7, *K6* Kessler Psychological Distress Scale, *cpd* cycles per degree

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

[a] Reflects pattern glare scores during exposure to the pattern with mid-spatial frequency (i.e., 2.3 cpd)

GAD-7, and K6) (Table 4). After controlling for all other significant predictors, it was found that Pattern 2 is statistically significant in predicting the mental health outcomes, including in PHQ-9 ($\beta = 1.07$, $t(97) = 3.26$, $p = 0.002$), GAD-7 ($\beta = 0.87$, $t(97) = 3.00$, $p = 0.003$), and K6 ($\beta = 0.75$, $t(97) = 2.55$, $p = 0.012$). As indicated by the $R^2$ value, the variance explained by each model is 43% for PHQ-9, 45% for GAD-7, and 42% for K6.

## Study 2: epidemiological youth sample

### Method

#### Participants

Between 14th August 2020 and 25th January 2022, a total of 530 young people were consecutively recruited as part

**Table 4** Multiple regression models for symptom outcomes at 3 months in the longitudinal community youth sample ($n = 104$)

| Baseline predictors | Outcomes at 3 months | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Depressive symptoms (PHQ-9) | | | Anxiety symptoms (GAD-7) | | | Psychological distress (K6) | | |
| | $\beta$ | $t$ | $p$ | $\beta$ | $t$ | $p$ | $\beta$ | $t$ | $p$ |
| Age | 0.11 | 0.49 | 0.626 | 0.34 | 1.73 | 0.088 | 0.27 | 1.36 | 0.176 |
| Total years of education | 0.19 | 0.76 | 0.448 | − 0.04 | − 0.19 | 0.852 | − 0.002 | − 0.008 | 0.994 |
| Days of no functioning due to distress | 0.36 | 3.73 | **< 0.001*****| 0.41 | 4.80 | **< 0.001***** | 0.28 | 3.35 | **0.001**** |
| Hopelessness (BHS) | 0.25 | 2.12 | **0.037*** | 0.05 | 0.45 | 0.651 | 0.27 | 2.57 | **0.012*** |
| Loneliness (UCLA) | 0.15 | 2.78 | **0.007**** | 0.13 | 2.88 | **0.005**** | 0.12 | 2.54 | **0.013*** |
| Visual stress (pattern 2)[a] | 0.72 | 3.26 | **0.002**** | 0.87 | 3.00 | **0.003**** | 0.75 | 2.55 | **0.012*** |
| | $F$ | $R^2$ | $p$ | $F$ | $R^2$ | $p$ | $F$ | $R^2$ | $p$ |
| Overall model | 12.34 | 0.43 | **< 0.001***** | 13.01 | 0.45 | **< .001***** | 11.63 | 0.42 | **< 0.001***** |

Bold values denote statistical significance at the $p < 0.05$ level

*PHQ-9* Patient Health Questionnaire, *GAD-7* Generalized Anxiety Disorder—7, *K6* 6-item Kessler Psychological Distress Scale, *BHS* Beck Hopelessness Scale, *UCLA* UCLA Loneliness Scale

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

[a]Reflects pattern glare scores during exposure to the pattern with mid-spatial frequency (i.e., 2.3 cpd)

of a larger ongoing household-based epidemiological youth mental health study in Hong Kong (HK-YES). The HK-YES is to date the first territory-wide study targeting youth mental health in Hong Kong. A stratified multistage cluster sampling design is adopted to improve representativeness. Specifically, randomly selected addresses were obtained from the local government and clustered by districts and housing types. All young people aged between 15 and 24 at the time of recruitment were invited through letters mailed to these addresses. Details regarding the HK-YES have also been reported elsewhere [19, 20].

### Study design and assessments

This was a cross-sectional study of 530 young people from a representative sample in Hong Kong. Findings from the current study can offer information in addition to those presented in Study 1 to validate the significance of visual stress in mental health.

As with Study 1, visual stress was also assessed using the Pattern Glare Test [2]. Other potential factors associated with mental health also included (1) the total number of days of having no functioning due to emotional distress (assessed using an item from the Sheehan Disability Scale [21]), resilience (CD-RISC-10) [15], hopelessness (BHS) [16], and loneliness (UCLA Loneliness Scale) [17].

### Clinical outcomes

In this study, the primary outcomes of mental health symptoms were assessed using the Depression, Anxiety and Stress Scales (DASS-21) [22] for depressive, anxiety, and stress symptoms and the K6 [16] for distress symptoms. The DASS-21 is a 21-item measure of symptoms of common mental disorders, which consists of three 7-item subscales for assessing symptoms of depression, anxiety, and stress (DASS-D, DASS-A, and DASS-S, respectively). Items were rated on a 4-point Likert scale (from 0 = "Did not apply to me" to 3 = "Applied to me very much") based on their experiences "in the past week". Composite scores were determined by multiplying the sum of items by a value of 2 for each of the subscales (range = 0–42), with a higher score indicating greater severity.

### Statistical analysis

All analyses were carried out in IBM® SPSS® Version 26.0. The level of statistical significance for all analyses was set at $p < 0.05$. The relationships between pattern scores on the Pattern Glare Test and symptom outcomes were analyzed using Spearman's rank correlation. Comparisons between scores on each of the patterns were also assessed using the Mann–Whitney *U* test. To further determine the associations between visual stress and symptom outcomes, separate multiple regression analyses were performed for each of the four symptom outcomes (symptoms of depression, anxiety, stress, and psychological distress). As with Study 1, basic demographic variables (age, gender, total years of education) as well as other correlates of symptom outcomes (including days of no functioning, resilience, hopelessness, and loneliness) were also accounted for in all regression models. Pattern 2 scores were included in the regression models as the key measure of visual stress.

## Results

Among participants of the epidemiological youth sample ($n = 530$), the mean age of participants was 19.7 years ± 2.83 years (standard deviation, SD), with 46.8% ($n = 248$) being male. The sample had a mean education of 13.3 years (± 2.40 years). Most of the participants were students at the time of assessment (77.9%, $n = 413$), while 18.5% ($n = 98$) reported being currently employed and 3.6% ($n = 19$) were currently unemployed. The mean and SD of resilience in these participants were 23.1 ± 6.46.

Pattern glare score was also significantly lower on Pattern 1 (0.3 ± 0.67) compared to both Patterns 2 (1.5 ± 1.31) and 3 (1.2 ± 1.29), both $p < 0.001$. Pattern 2 also had a significantly higher pattern score compared to Pattern 3, $p < 0.001$.

### Associations between visual stress and mental health symptoms in the epidemiological youth sample

Regarding their symptom levels, the means and SDs were 9.61 ± 8.68 for DASS-D, 7.48 ± 7.52 for DASS-A, 10.71 ± 8.69 for DASS-S, and 8.01 ± 5.37 for K6.

Findings from the univariate analyses revealed significant mild associations between Pattern 2 score and depressive symptoms (DASS-D: $r_s = 0.19$), anxiety symptoms (DASS-A: $r_s = 0.20$), stress symptoms (DASS-S: $r_s = 0.19$), and psychological distress (K6: $r_s = 0.18$), all $p < 0.001$. Furthermore, the multiple regression analyses revealed that, even after accounting for age, years of education, as well as functioning and other psychological factors, Pattern 2 continued to show significant associations with all symptom outcomes: DASS-D ($\beta = 0.09$, $p = 0.006$), DASS-A ($\beta = 0.13$, $p = 0.001$), DASS-S ($\beta = 0.09$, $p = 0.011$), and K6 ($\beta = 0.08$, $p = 0.021$). More days of no functioning, lower resilience, higher hopelessness, and higher loneliness were also associated with all four symptom outcomes (all $p < 0.05$).

## Discussion

The relationship between visual stress and common mental disorders has rarely been explored in the literature before. The current study aimed to examine the clinical use of visual stress as a predictor of youth mental health outcomes in larger samples than in previous studies. As the first to administer the Pattern Glare Test to participants in Hong Kong, we hope to provide a reference for the generalizability of results related to visual stress not only in Hong Kong but also across cultures. Using two separate community and epidemiological youth samples, we provided the first pieces of evidence to show that Pattern 2 can produce greater visual stress among young participants. Importantly, even when other significant correlates of symptom outcomes were accounted for, visual stress to Pattern 2 at baseline significantly predicted more severe depressive symptoms, anxiety symptoms, as well as psychological distress (K6) not only cross-sectionally but also longitudinally at 3 months. It is interesting to note that the effect of Pattern 2 in the multivariate model in the longitudinal community sample (Study 1), where other common mental health factors were controlled for, was stronger than is evident for its bivariate correlates with the 3-month outcome measures. This suggests that pattern glare has a strong and unique effect that may be disparate from the common mental health predictors.

### Comparison with previous research

Our finding that Patterns 2 and 3 with 2.3 and 9.4 cpd, respectively, will stimulate more illusions than Pattern 1 with 0.3 cpd is consistent with previous findings [3]. However, while slightly higher scores were previously found for Pattern 3 than Pattern 2, the opposite trend was observed in the current studies. Indeed, the existing literature has suggested that patterns with an SF of 2.3 cpd could elicit maximum pattern glare responses. It has also been described in the original studies that Patterns 1 and 3 were designed as control stimuli in the Pattern Glare Test, whereby Pattern 1 responses are indicative of suggestibility while Pattern 3 responses are more reflective of optical rather than neurological mechanisms [1, 3, 22]. We had therefore utilized pattern glare responses toward Pattern 2 as our key measure of visual stress-related cortical excitability in our multivariable analyses in both studies.

In line with our hypothesis, visual stress was significantly associated not only with cross-sectional but also prospective symptoms of depression and anxiety, as well as psychological distress, after 3 months. The current findings are consistent with a previous study in which patients diagnosed with MDD expressed greater pattern glare to Pattern 2 than healthy controls [10]. However, their categorical approach may have limited the practicability of their findings, as the etiology and the clinical manifestation of mental health conditions are typically multifactorial and heterogeneous. Given the common co-occurrence of mental health symptoms, identifying a marker for a single mental health disorder can be difficult, if not impossible. In addition, the quality of a clinical formulation for diagnoses such as MDD positive and MDD negative is heavily dependent on the characteristics of both the patient and the disorder, which can be difficult to establish [23]. Taking a dimensional approach, as in the current studies, may therefore be more relevant in hypothesis testing, particularly when working with community- and population-based samples.

### Possible mechanisms behind visual stress and symptoms

The mechanisms driving the relationship between visual stress and symptoms of common mental disorders and distress have yet to be explored. However, it has been hypothesized to be due to a lack of cortical inhibition, or cortical hyperexcitation, related to a failure in GABAergic inhibition in the occipital cortex [6, 10]. According to the GABAergic-deficit hypothesis, reduced concentration of the inhibitory neurotransmitter GABA is an important factor in the etiology of mood disorders such as MDD and particularly anxiety [24]. Indeed, research examining mood disorders has found a dramatic reduction in GABA occipital cortex, as well [9]. Therefore, susceptibility to pattern glare may reflect an abnormality in the GABA system (e.g., cortical hyper-excitability) that also predisposes to the experience of mood disorders.

Notably, the symptoms we considered in the current studies are those that are typically considered to lie on the internalizing disorder spectrum [25, 26]. While our findings generally showed that the effect of visual stress on anxiety symptoms may be slightly stronger as compared to other symptom outcomes, the observation that visual stress is also significantly associated with depressive, stress, and distress symptoms suggests there exists an at least partially common pathway underlying their pathogeneses. These findings would be in line with the growing literature on the identification of transdiagnostic markers for predicting mental disorders and may offer some additional insights into the high rates of comorbidity observed across psychiatric disorders [27, 28]. Whether and how visual stress may also be implicated in other symptom outcomes, including those on the psychotic and externalizing disorder spectrum, remain to be investigated in future studies.

### Factors other than visual stress

Analyses showed other significant predictors beyond visual stress that were related to depression, anxiety, and psychological distress: reduced functioning due to emotional distress, hopelessness, and loneliness. Indeed, psychiatric disorders such as MDD and GAD are characterized by difficulties in functioning across social, financial, occupational, and physical domains [29]. A bi-directional negative relationship has been found between mental health outcomes and education, employment, or training (NEET) in youths [30]. The interference of psychiatric symptoms with everyday functioning may be related to the cognitive deficits that are commonly present in those disorders, such as deficits in memory [31] and executive functioning [32]. Such impairments in functioning may further increase frustration and reinforce vulnerability to mental health issues.

The current study also suggests hopelessness to be a marker of depression even after 3 months. According to the cognitive content-specificity hypothesis [33], depression is uniquely related to dysfunctional cognitions such as the tendency to perceive the future in a more pessimistic manner. In contrast, cognitive content in anxiety was theorized to be threat orientated. Supporting evidence for this has been provided by studies that found hopelessness to predict future symptoms of depression 4 weeks later—although anxiety could not be predicted from hopelessness [34]. The specificity of hopelessness to depression may partially explain why although correlated, hopelessness failed to predict symptoms of anxiety when other variables were also considered in the analysis.

Finally, loneliness was a predictor of symptoms of depression, anxiety, and psychological distress, too. As loneliness is likely the result of social isolation or the lack of social relations, there may be fewer sources of social support available for lonely individuals. In this way, loneliness may impair one's resilience by eliminating an effective coping mechanism involving support-seeking and active coping [35]. The benefits of friendships also extend to promoting one's self-efficacy, self-esteem, emotional intelligence, and many other areas [36]—all of which may have important implications on mental health. Certainly, studies have also supported loneliness as an important social factor for both anxiety and depression [37].

## Limitations

The current studies have shed light on the relationship between visual stress and symptoms of common mental disorders. Despite the unique insight into the relationship between symptoms of common mental disorders and visual stress, we acknowledge that our studies are lacking in the measure of conditions related to visual stress (e.g., migraine, trypophobia, autism, and attention deficit hyperactivity disorder features). Future studies should assess these factors to elucidate the associations between visual stress and symptom severity, while controlling for these potential confounding factors in a comprehensive and rigorous manner. Future research could also explore the relationship from a neurological perspective to examine whether GABAergic deficits underlie the linkages between them. More vigorous experimental design could be adopted to assess the nature of relationship between visual stress and mental health, to evaluate the value of the Pattern Glare Test in understanding and assessing mental health issues. In addition, while we consider it important to examine the symptoms from a dimensional perspective, it may also be helpful in future research to consider whether visual stress may act as a marker also for specific subtypes of depressive and anxiety disorders (e.g., bipolar vs unipolar depression) to guide early risk detection and intervention strategies.

## Conclusion

In densely populated and competitive cities like Hong Kong, young people face a variety of emerging risk factors that simply did not exist in previous generations. This has resulted in rapidly increasing levels of depression, anxiety, loneliness, suicidal ideation, as well as plummeting life satisfaction and well-being. The successful identification of visual stress as a marker of cortical hyper-excitability in predicting mental health symptoms can bring about far-reaching influences in the screening and prediction of potential risks of mental disorders at community and population levels. Given the simplicity of its assessment, the confirmation and validation of visual stress in relation to mental health could be helpful in the development of interventions in the future, especially with further understanding of its underlying mechanisms. Adopting visual stress as a quick screening tool for those at risk could also provide a framework for dialogue and discussions between professionals and young people on sensitive mental health topics.

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**Author contributions** EYHC conceived and designed the study. TYTY, TTYL, OCYC, and ST performed data collection. EYHC, CLMH, SMYW, and TYTY analyzed the data. EYHC, CLMH, SMYW, TYTY, and AW interpreted the results. All authors reviewed and validated the

data. CLMH, SMYW, and TYTY wrote the initial draft and completed initial revisions of the manuscript. All authors provided critical input to the drafts of the manuscript and approved the final manuscript.

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**Availability of data and materials** Data are available upon reasonable request.

## Declarations

**Conflict of interest** EYHC reports having received speaker honoraria from Otsuka and DSK BioPharma; received research funding from Otsuka; participated in paid advisory boards for Jansen and DSK BioPharma; received funding to attend conferences from Otsuka and DSK BioPharma. The remaining authors declare no competing interests.

**Ethics approval** Both studies were approved by the Institutional Review Boards of the University of Hong Kong/Hospital Authority Hong Kong West Cluster and carried out in accordance with Good Clinical Practice and the Declaration of Helsinki.

**Consent to participate** Written informed consent was obtained from all participants.

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