# Magnocellular and Parvocellular Mediated Luminance Contrast Discrimination in Severe Alcohol Use Disorder

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**Background:** Severe alcohol use disorder (SAUD) is associated with widespread cognitive impairments, including low-level visual processing deficits that persist after prolonged abstinence. However, the extent and characteristics of these visual deficits remain largely undetermined, impeding the identification of their underlying mechanisms and influence on higher-order processing. In particular, little work has been conducted to assess the integrity of the magnocellular (MC) and parvocellular (PC) visual pathways, namely the 2 main visual streams that convey information from the retina up to striate, extrastriate, and dorsal/ventral cerebral regions.

**Methods:** We investigated achromatic luminance contrast processing mediated by inferred MC and PC pathways in 33 patients with SAUD and 32 matched healthy controls using 2 psychophysical pedestal contrast discrimination tasks that promote responses of inferred MC or PC pathways. We relied on a staircase procedure to assess participants' ability to detect small changes in luminance within an array of 4 gray squares that were either continuously presented (steady pedestal, MC-biased) or briefly flashed (pulsed pedestal, PC-biased).

**Results:** We replicated the expected pattern of MC and PC contrast responses in healthy controls. We found preserved dissociation of MC and PC contrast signatures in SAUD but higher MC-mediated mean contrast discrimination thresholds combined with a steeper PC-mediated contrast discrimination slope compared with healthy controls.

**Conclusion:** These findings indicate altered MC-mediated contrast sensitivity and PC-mediated contrast gain, confirming the presence of early sensory disturbances in individuals with SAUD. Such low-level deficits, while usually overlooked, might influence higher-order abilities (e.g., memory, executive functions) in SAUD by disturbing the "coarse-to-fine" tuning of the visual system, which relies on the distinct functional properties of MC and PC pathways and ensures proper and efficient monitoring of the environment.

**Key Words:** Alcohol Use Disorder, Vision, Visual Pathways, Magnocellular, Parvocellular.

VISUAL PROCESSING DE ficits, together with widespread cognitive and emotional impairments, have long been described among patients with severe alcohol use disorder (SAUD) (Bernardin et al., 2014; Oscar-Berman et al., 2014; Rolland et al., 2019; Stavro et al., 2013). The interest for visual processing in SAUD emerged from the observation that patients are often impaired in routinely used neuropsychological tasks requiring efficient visual analysis, such as the Rey-Oestherith Complex Figure copy or the WAIS Block Design and Object Assembly subtests (e.g., Beatty et al., 1997; Fitzhugh et al., 1960, 1965; Jones, 1971; Wilson et al., 1988). Subsequent studies confirmed the presence of visual impairments by measuring visual evoked potentials, chromatic and achromatic vision, motion and speed processing, or peripheral visual field perception (Creupelandt and Maurage, 2021). They also showed that visual processing deficits may persist with long-term abstinence, inducing durable perceptual changes (da Cruz et al., 2016; Fein et al., 1990, 2006; Yohman et al., 1985).

However, the processing stage at which these visual deficits occur remains undetermined. Beyond the general description of structural and functional impairments in broad cerebral regions supposed to be associated with visual processing (e.g., Kril et al., 1997; Tapert et al., 2003), few studies have explored specific visual functions. The heterogeneity of previous experimental paradigms and their reliance on multiple cognitive processes prevented precise conclusions regarding the integrity of the visual system. Visual disturbances in

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SAUD might start at the eye structure level (e.g., retina, optic nerve), at the lateral geniculate nucleus (LGN) relays, and/or involve striate, extrastriate, or even higher-level cerebral damage. This question is critical to understand the mechanisms underlying widespread higher-order processing deficits in SAUD, as low-level visual deficits might impair the subsequent cognitive and emotional stages, and patients with SAUD may have to base their decisions and judgments on degraded visual information (Creupelandt et al., 2019). Besides, recent theoretical frameworks (Firestone and Scholl, 2016; Newen and Vetter, 2017; O'Callaghan et al., 2017) postulate early connections between the visual system and higher-level cerebral areas (e.g., orbitofrontal cortex) implicated in a variety of crucial executive and emotional processes (Bar, 2003; Kauffmann et al., 2015; Kveraga et al., 2007). Applying such models to SAUD would thus renew the understanding of visual impairments, as well as their influence on the largely explored high-level cognitive functions (Creupelandt et al., 2019). Importantly, these models rely on the distinct but complementary functions of the anatomically separated magnocellular (MC) and parvocellular (PC) pathways (Kravitz et al., 2011, 2013). They posit that the "coarse-to-fine" visual analysis supported by these pathways, together with the input from higher-order cerebral regions, allows the computation of quick predictions regarding the identity, emotional content, and adaptative values of surrounding visual stimuli (Panichello et al., 2013).

The MC and PC visual pathways are thought to originate at the level of the retinal ganglion cells and to sustain parallel visual processing up to at least the visual primary cortex (V1) (Dacey, 2004; Merigan and Maunsell, 1993; Nassi and Callaway, 2009). The MC pathway relies on parasol ganglion cells, which correspond to approximately 10% of the total population of cells that project to the LGN, and carries a broadband achromatic signal to the MC layers of the LGN and layers 4Cα and 6 of V1 (Blasdel and Lund, 1983; Dacey, 2000). Cells in the MC pathway have large receptive fields, fast axonal conduction velocities, and are sensitive to high temporal frequencies as well as low spatial frequencies (i.e., coarse/global information) (Livingstone and Hubel, 1988). They exhibit specific responses to luminance contrast (i.e., the difference in luminance distinguishing different visual inputs), an important low-level visual property associated with object detection and recognition, as well as perceptual decision making ('t Hart et al., 2013). Indeed, cells in the MC pathway show high luminance contrast sensitivity: They respond to low contrasts but saturate with high contrasts (Kaplan and Shapley, 1986; Plainis and Murray, 2005). Conversely, the PC pathway relies on midget ganglion cells, which engage approximately 80% of the total population of cells that project to the LGN, and carries a red/green color opponent signal to the PC layers of the LGN and layers 4Cβ and 6 of V1 (Blasdel and Lund, 1983; Dacey, 2000). Cells in this pathway have small receptive fields, slow axonal conduction velocities, and are sensitive to low temporal frequencies and high spatial frequencies (i.e., fine/detailed information) (Livingstone and Hubel, 1988). They show low contrast sensitivity and thus respond at a higher rate to moderate and high contrasts compared with low ones (Kaplan and Shapley, 1986; Plainis and Murray, 2005). Both types of retinal ganglion cells peak close to the fovea and decline toward the periphery, contributing to both central and peripheral vision (Grünert et al., 1993; Grünert and Martin, 2020; Silveira and Perry, 1991). Whether the MC and PC pathways remain strictly segregated or are intermixed within V1 is still a matter of debate, with evidence suggesting either that (i) early parallel pathways of the retina and LGN could be reorganized within V1 into spatial and cell type-specific modules to form multiple output channels for extrastriate areas (Nassi and Callaway, 2009); or (ii) specific MC and PC pathways exist and extend through dedicated columns in early and middle stages of the extrastriate cortex (Tootell and Nasr, 2017). What appears clearer is that the outputs from V1 and the second visual area (V2) to the middle temporal visual area (MT or V5) and the fourth visual area (V4), specialized in motion/depth processing and form/color processing, respectively, represent the beginning of 2 separated but interacting parallel visual streams, generally referred to as the "dorsal" and "ventral" streams (Kravitz et al., 2011; Merigan and Maunsell, 1993). The dorsal and ventral streams, broadly associated with parietal and temporal regions, are notably thought to drive spatial localization and object recognition. Clear cross talks however exist between them, from connections between MT and V4 and onwards (Nassi and Callaway, 2009), so that the dorsal and ventral streams interact to inform each other. On this basis, it has been proposed that feedback connections from the parietal and temporal cortex, potentially of primary MC origin due to the fast axonal conduction velocity of MC cells (Bullier et al., 1996; Schmolesky et al., 1998), could carry signals to be retroinjected into lower-order areas (Bullier, 2001; Chen et al., 2007). This mechanism is thought to help to deal with the continuous flow of incoming visual information and to improve the processing of the slower incoming PC-related cues (Bar, 2003; Barrett and Bar, 2009; Kauffmann et al., 2015; Kveraga et al., 2007).

Studies on acute alcohol consumption have suggested that alcohol selectively impairs the MC pathway, leaving the PC pathway preserved (Hill and Toffolon, 1990; Khan and Timney, 2007). Acute alcohol intakes indeed (a) reduce temporal contrast sensitivity at high temporal frequencies (Pearson and Timney, 1998); (b) slow down neural processing and transmission speed (Khan and Timney, 2007); and (c) affect visual sensorimotor functions and visual fields while leaving acuity, color vision, and stereoacuity unaffected (Hill and Toffolon, 1990). While these results cannot be directly applied to SAUD, deficits for global rather than local visual processing (Beatty et al., 1997; Daig et al., 2010; Kramer et al., 1989, 1991; Robertson et al., 1985), combined with evidence of reduced motion processing (Chambers and Wilson, 1968; Wegner et al., 2001) and lower temporal sensitivity (Pillunat et al., 1985; Williams, 1984) also suggest that the

MC pathway may be impaired in SAUD. This proposal is also partly consistent with more indirect neuroimaging results revealing a different pattern of activation of the ventral (overactivation) and dorsal (underactivation) visual streams in SAUD during a spatial working memory task: Individuals with SAUD could thus rely on extra ventral activation to compensate for dorsal alterations (Pfefferbaum et al., 2001; Tapert et al., 2001). Direct experimental evidence is nonetheless lacking to confirm this MC/PC dissociation proposal in SAUD as the integrity of MC and PC pathways in SAUD has not yet been assessed through a single experimental paradigm specifically designed to dissociate the 2 pathways while limiting the influence of concurrent higher-order cognitive processes.

Our purpose was to test the proposal of a differential deficit between MC and PC pathways in SAUD. To do so, we investigated whether SAUD is associated with impairments in contrast processing mediated by the MC and PC pathways using a well-documented psychophysical task dissociating these pathways through their distinct low-level achromatic luminance contrast properties (for a review, see Pokorny, 2011). More precisely, we compared the performances of recently detoxified individuals with SAUD and healthy controls (HC) in an adapted version (Zhuang et al., 2012) of the steady and pulsed pedestal paradigms (Pokorny and Smith, 1997). These paradigms exploit the distinction between MC and PC functioning by promoting the processing of low and high luminance contrasts, respectively. Considering that the MC pathway shows high contrast sensitivity (i.e., responds to low contrasts but rapidly saturates for high contrasts), whereas the PC pathway shows low contrast sensitivity (i.e., demonstrates a higher response rate to moderate and high contrasts compared with low ones; Kaplan and Shapley, 1986), this manipulation supports the differing MC and PC contrast signatures and allows to bias visual processing toward one or the other pathway. Based on previous work proposing selective primary MC deficits, we expected individuals with SAUD to display impaired MC and preserved PC-mediated contrast properties. We thus hypothesized that they would show higher contrast discrimination thresholds than HC in the steady but not pulsed pedestal task.

## MATERIAL AND METHODS

### *Participants*

We recruited 33 individuals diagnosed with SAUD according to DSM-5 criteria (American Psychiatric Association, 2013) who were following an in-patient alcohol-treatment program in 2 Belgian hospitals (Clinique Saint-Pierre Ottignies and Le Beau Vallon) (see Table 1). Patients had been abstinent for a minimum of 9 days at the testing time and had to be free of any other psychiatric diagnosis, except tobacco use disorder. To ensure that our results would not reflect short-term visual changes strictly due to alcohol-withdrawal and related medication, the testing took place at the end of the residential detoxification program, when the initial benzodiazepine treatment was generally discontinued. Despite this precaution, 10 patients were still administered benzodiazepines at the time of the testing. The average dose of benzodiazepine (diazepam or lormetazepam) for these patients was 14.33 (SD = 13.41) mg/day. Patients with SAUD were matched with 32 healthy controls (HC), free of any history of psychiatric disorder. They consumed less than ten standard alcohol units per week—1 standard alcohol unit corresponding to 10g of pure EtOH—and never exceeded 3 standard units per day. HC had to refrain from drinking any alcohol during the 72 hours before testing and were financially compensated for their participation. Exclusion criteria for both groups included any ophthalmologic and/or neurological disease, as well as severe head traumas. All participants reported normal hearing and normal or corrected-to-normal vision.

We collected complementary self-reported measures of participants' alcohol consumption patterns through the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) and used a cut-score of 8 to ensure the absence of risky consumption in HC. We also reported education levels, corresponding to the number of years of education completed since starting primary school, and screened participants for depression/anxiety symptoms with the Beck Depression Inventory (BDI-II; Beck et al., 1996) and the State and Trait Anxiety Inventory, form A and B (STAI-A and B; Spielberger et al., 1983). We gathered patients' daily dosage of benzodiazepines at the testing time through their medical records.

The biomedical ethics committee of UCLouvain approved the study (approval number: B40320173402), which was carried out according to the principles of the Declaration of Helsinki. All participants gave their written informed consent before inclusion in the study and were tested individually.

### *Apparatus and Stimuli*

The experiment was conducted on a gamma-corrected Dell M783p 17" CRT color monitor with a refresh rate of 85Hz, controlled by a Dell Latitude 5580 laptop. The Intel(R) HD Graphics 620 graphic card of the laptop provided a resolution of 8 bits for each of the 3-color guns of the 1024*768 pixels CRT display. The CRT monitor was calibrated using a Minolta LS-100 photometer, and luminance values were linearized with look-up tables. We generated and presented stimuli using the coder view of PsychoPy v3.0.1 (Peirce, 2007). Participants seated 57 cm away from the screen in a

**Table 1.** Group characteristics for Individuals with Severe Alcohol Use Disorders (SAUD) and Healthy Controls (HC): Mean (SD)

| | SAUD ($N = 33$) | HC ($N = 32$) |
|---|---|---|
| *Demographic measures* | | |
| Gender ratio (M/F)$^{NS}$ | 15/18 | 13/19 |
| Age (in years)$^{NS}$ | 45.3 (10.9) | 44.4 (8.0) |
| Education (in years)$^{***}$ | 12.9 (2.4) | 16.7 (2.9) |
| *Alcohol and tobacco-related measures* | | |
| DSM-5 criteria | 8.6 (1.6) | NA |
| Alcohol units per day$^{***}$ | 27.1 (19.0) | 0.2 (0.2) |
| Years of SAUD | 8.4 (7.5) | NA |
| Duration of abstinence (days) | 19.0 (7.4) | NA |
| No. of previous detoxifications | 1.7 (1.8) | NA |
| AUDIT score$^{***}$ | 29.0 (6.0)[a] | 1.9 (1.6) |
| Benzodiazepine dosage (mg/day) | 3.9 (9.2) | NA |
| No. of cigarettes per day$^{***}$ | 17.6 (14.9) | 0.0 (0.0) |
| *Psychopathological measures* | | |
| BDI-II$^{***}$ | 23.7 (12.3)[a] | 6.0 (7.3) |
| STAI-A (state)$^{***}$ | 44.6 (13.7)[b] | 29.2 (8.5) |
| STAI-B (trait)$^{***}$ | 55.8 (10.4)[a] | 35.0 (10.4) |

AUDIT, alcohol use disorders identification Test; BDI-II, Beck Depression Inventory; STAI-A and B, State and Trait Anxiety Inventory.

NA, not applicable; NS, nonsignificant; $^{***}p < 0.001$.

[a]2 missing data.

[b]1 missing data.

dark room, ensuring a constant ambient luminance. The background of the screen was set to 15.5 cd/m$^2$ throughout the experiment.

Stimuli consisted of a pedestal, that is, a 2 × 2 array of 4 squares, systematically presented at the center of the screen. Each of the 4 squares sustained a visual angle of 1°×1° (1cm on screen) and was separated by a line (0.1°). A fixation cross (0.1° × 0.1°) was presented at the center of the screen during the whole experiment.

### *Tasks and Procedures*

*Steady and Pulsed Pedestal Paradigms.* At the beginning of both pedestal paradigms, participants were presented with the fixation cross for 1 minute, as an adaptation period to the background luminance. In the steady pedestal, this adaptation period was followed by a 5-second adaptation to the luminance of the pedestal. Then, each experimental trial started with an adaptation to the pedestal luminance (1.2 s) followed by a short test interval (35.29 ms) during which the luminance of 1 target square, randomly chosen between the 4, was increased. Participants had to press 1 of 4 buttons on a numerical pad to indicate which of the 4 squares had briefly changed compared with the others. A response was required for every trial.

In the pulsed pedestal, the experimental trials started directly after the 1-minute background adaptation period. Pulsed trials were similar to steady ones, except that only the fixation cross was shown (1.2 s) before the pedestal appeared. The pedestals were thus only visible during the short test interval (35.29 ms), with 1 of the squares being brighter. By removing the adaptation period to the pedestal luminance, participants were no longer able to rely on the difference in luminance between the pedestal and target square and were instead forced to deal with higher contrasts resulting from the comparison between target square and background. Such high contrasts saturate the MC pathway so that contrast discrimination in pulsed trials is mediated by the PC pathway (Pokorny and Smith, 1997).

Given the attentional demand of the task, and as SAUD is associated with attentional impairments, we added a brief (110 ms) warning sound 600 ms before the test interval in both conditions, to promote efficient attentional preparation and inform the participant of the visual change occurring. Figure 1 illustrates the time course of a trial in both pedestal paradigms.

We divided the steady and pulsed paradigms into 5 and 4 experimental blocks, respectively, defined by the distinct luminance values of the pedestals. We used 5 luminance values for the steady paradigm: 15.5, 18.9, 24.5, 29.9, and 37.7 cd/m$^2$. They corresponded to Weber contrasts of 0%, 22%, 58%, 93%, and 143%, respectively, Weber contrast defined as $C_w = (L_{pedestal} - L_{background})/L_{background}$. We used the same values in the pulsed paradigm, excepted for 15.5 cd/m$^2$. At this specific value, pedestal contrast was 0 as the luminance of the pedestal matched that of the background. Hence, participants only saw 1 square (i.e., the target square) appearing on screen during the test interval. The MC pathway mediates thresholds resulting from this condition because of its higher contrast sensitivity compared with the PC pathway (Pokorny and Smith, 1997). All other pedestals presented higher luminance than the background.

We applied an adapted "2-down, 1-up" staircase procedure to each experimental block. Following Zhuang et al. (2012)'s methodology, the first change in luminance of the target square consisted of a very large increment approaching $10^{0.2}$ × the pedestal luminance. This initial luminance step size was then divided by $\sqrt{2}$ every time the participant correctly detected the target square, until a minimum step size, matching the limitations of the screen display properties in terms of color depth, was reached. We adjusted these theoretical values according to material constraints using the photometer, resulting in 10 different step sizes (i.e., 10 levels of increasing difficulty) of 59.52, 39.27, 26.75, 18.32, 12.84, 9.02, 6.86, 4.98, 3.39, and 1.57% higher luminance, respectively. This slightly adapted methodology led to the introduction of 4 additional step sizes (39.27%, 18.32%, 9.02%, and 4.98%) compared with Zhuang et al. (2012), allowing to detect more inter-individual variability at relatively high contrasts (≥4.98%). By comparison, we could not increase the number of step sizes at relatively low contrasts (<4.98%).

While difficulty initially increased following correct responses, generating the use of smaller step sizes, each erroneous response led to a change in the staircase direction: the difficulty level decreased after an error, leading to the presentation of the previous, hence larger and easier, luminance step size. Two correct responses in a row at the same luminance step size were required for the staircase to go down again and step sizes to be reduced. The staircase procedure stopped after the participant either: (a) alternated 5 "ups and downs" (i.e., 5 errors each followed by 2 consecutive correct responses, leading to a "plateau" performance); and (b) made 5 consecutive correct responses at the minimum step size (1.57%). On average, participants reached the stop rule after 30 trials (SD = 5.5, range: 14–52). The contrast discrimination threshold for each specific experimental block corresponded either to the mean value of the last 3 "plateau" or to the minimum value of 1.57% (reached in 6.7% of all experimental blocks). Consistent with most psychophysical studies and Zhuang et al. (2012)'s procedure, thresholds in percentages of luminance were then converted into cd/m$^2$ according to the distinct luminance values of each pedestal, before being log-transformed (base 10) for further analyses and visual plotting.

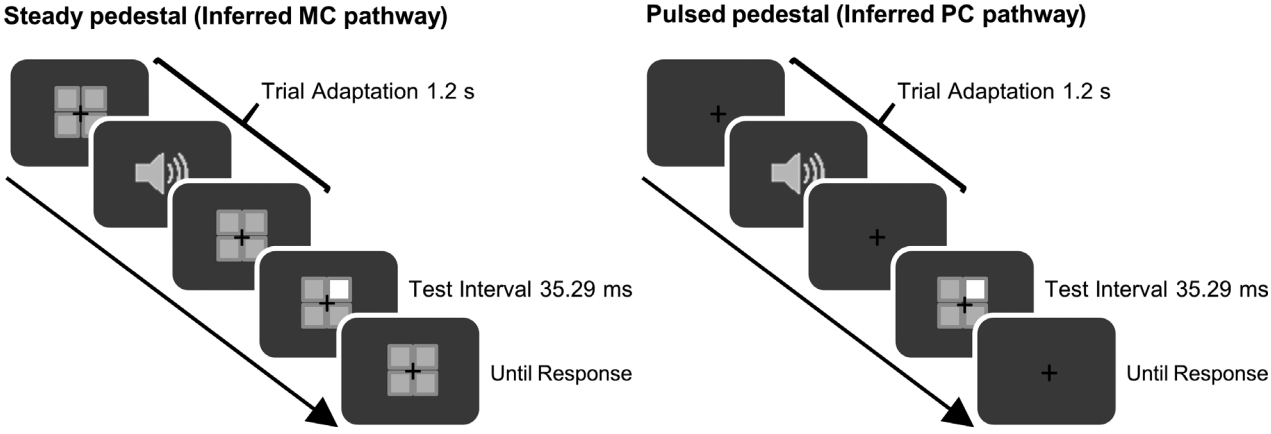


**Fig. 1.** Illustration of the time course of 1 trial in the steady and pulsed pedestal conditions.

We ran pilot sessions on 10 individuals to pretest the parameters of the staircase and ensure an efficient threshold measurement. We randomized the order of the steady and pulsed paradigms across participants, as well as the pedestal luminances within each paradigm. Participants completed the self-reported psychological and alcohol-related questionnaires in between both paradigms.

*Complementary Visual and Attentional Control Subtasks.* We checked participants' acuity and general contrast discrimination using the Freiburg Visual Acuity Test (FrACT version 3.9.9a; Bach, 1996, 2007) before the experimental tasks. The acuity task measured participants' spatial resolution limits based on the detection of the orientation of Landolt Cs of varying sizes. Results, in logMAR units, express the logarithm of the Minimum Angle of Resolution in minutes of arc. A score of 0 logMAR reflects "normal vision" and the better the acuity, the lower the logMAR value. The contrast sensitivity task used similar Landolt Cs, mixing low to medium spatial frequencies, but made their luminance vary with respect to the background. Results, reported in Weber contrast values, represent the minimum difference in luminance between the background and Landolt Cs (in percentage) that one can distinguish.

To control for possible attentional fluctuations and guarantee that patients can process very quick (35.29 ms) visual changes, experimental sessions ended with 2 short subtasks mimicking the format of the pulsed and pedestal paradigms, respectively, without requiring high-level visual processing. Each subtask comprised a fixed number of 50 trials (i.e., the maximum number of trials generally required to reach the stop rule in the pedestal paradigms) and participants followed the same instructions (i.e., detect the square whose luminance changed). Compared with the actual pulsed and steady pedestals, there was no staircase procedure and the pedestal and target square luminances were continuously set to 26 cd/m$^2$ (≈mean value between the lowest and highest pedestal values used in the experimental paradigms) and 41.8 cd/m$^2$ (corresponding to + 62% luminance), respectively. We chose these fixed values to ensure a very low perceptual load and make it possible to interpret any error as an attentional lapse rather than a visual processing-related deficit.

*Data Analyses.* We conducted the analyses in R (version x64 3.6.0) with an alpha set to .05. We first performed between-group comparisons on demographic and psychopathological variables (see Table 1) using (i) Wilcoxon rank-sum tests and Welch's t-tests for quantitative variables depending on normality and homogeneity of variance assumptions; and (ii) Pearson chi-square tests for qualitative variables.

We then applied a linear-mixed model (LMM) to contrast thresholds through the "nlme" package (Pinheiro et al., 2020) with Group, Pedestal Condition, and Pedestal Luminance as fixed effects and participants as a random effect (random intercept). Pedestal luminance values were entered as a continuous variable to examine the slope of the luminance contrast discrimination function. The random factor for participants considered the dependence between our observations due to repeated measures while adjusting the intercept for each participant. Its significant contribution to the variance of the model was confirmed by a likelihood ratio test, ensuring model fit. Diagnostics of linearity, homoscedasticity, and normality of residuals and random effects ensured the absence of problems regarding the central assumptions of the model. Following Zhuang et al. (2012), we further screened residuals from the model to detect potential outliers and removed most extreme thresholds associated with residuals 3 standard deviations away from the mean. We then applied an additional analysis of variance using type III sum of squares to the LMM, assessing the global effects of each predictor. We calculated Bonferroni-corrected post hoc comparisons through the "emmeans" package (Lenth et al., 2020), by computing t-ratios based on the estimated marginal means from the LMM fitted to all data. Marginal and conditional $R^2$ values from the "piecewiseSEM" package (Lefcheck, 2016) measured the proportion of total variance explained by the fixed effects, and by both fixed and random effects. In addition to the LMM, we performed complementary analyses based on the modeling equations of Pokorny and Smith (1997) to ensure that our data and findings were consistent with the tasks' original framework. These analyses are available in Appendix S1.

Finally, we computed additional Wilcoxon rank-sum tests and Welch's t-tests to (i) compare group performances on general acuity and contrast results from the FrACT, as well as on pseudo steady and pulsed attentional tasks; and (ii) compare the pedestal thresholds and slopes of individuals with SAUD with and without benzodiazepine medication, and with or without tobacco use disorder. Pearson's and Spearman's correlations (corrected for multiple comparisons) assessed how alcohol consumption measures and nonalcohol-related variables associated with a group difference correlated with discrimination thresholds and slopes from pulsed and pedestal paradigms within individuals with SAUD.

## RESULTS

### *Demographic and Psychopathological Measures*

Patients with SAUD showed higher AUDIT scores ($W = 992$, $p < 0.001$), drank more alcohol ($W = 1056$, $p < 0.001$), and smoked more than HC ($W = 912$, $p < 0.001$). They displayed lower education levels ($W = 161$, $p < 0.001$) and higher depression ($W = 922.5$, $p < 0.001$) as well as state ($W = 865$, $p < 0.001$) and trait ($W = 899.5$, $p < 0.001$) anxiety scores. No significant group differences emerged for age, $t(58.76) = 0.38$, $p = 0.706$, and gender, $\chi^2(1) = 0.02$, $p = 0.886$.

### *Contrast Discrimination Thresholds and Slopes*

Four pulsed pedestal thresholds from individuals with SAUD qualified as outliers (2 reflecting extremely low thresholds, 2 reflecting extremely high thresholds) and were removed from the final LMM fit. Marginal and conditional $R^2$ values of the final model reached .85 and .89, respectively.

There was a significant main effect of Pedestal Condition, $F(1, 510) = 26.26$, $p < 0.001$, Pedestal Luminance, $F(1, 510) = 496.54$, $p < 0.001$, and Group, $F(1, 63) = 4.43$, $p = 0.039$, as well as significant interactions between Pedestal Condition and Pedestal Luminance, $F(1, 510) = 64.51$, $p < 0.001$, Pedestal Condition and Group, $F(1, 510) = 4.15$, $p = 0.042$, and Pedestal Luminance and Group, $F(1, 510) = 5.74$, $p = 0.017$. The three-way Pedestal Condition × Pedestal Luminance × Group also reached significance, $F(1, 510) = 3.88$, $p = 0.049$. Table 2 reports the estimates of post hoc comparisons in log luminance (cd/m$^2$) units. Individuals with SAUD and HC both displayed higher thresholds in the pulsed compared with the steady pedestal condition ($p < 0.001$). Thresholds also increased faster with higher pedestal luminance values in the pulsed than steady pedestal in both groups ($p < 0.001$). Concerning group differences, individuals with SAUD showed higher thresholds than HC in the steady ($p = 0.019$) but not pulsed ($p = 0.179$) pedestal condition, irrespective of luminance values. By contrast,

individuals with SAUD's thresholds increased faster than HC's ones with higher luminance values in the pulsed pedestal condition only (pulsed: $p = 0.034$; steady: $p = 1.000$). The slope of the luminance contrast discrimination function was thus steeper in individuals with SAUD than HC in the pulsed pedestal condition, whereas it increased similarly across groups in the steady pedestal condition despite systematically higher thresholds in individuals with SAUD in this condition. Figure 2 plots all participants' raw thresholds and illustrates the model fit for both groups and pedestal conditions. Thresholds are also plotted for each participant individually in Appendix S2.

### *Control Tasks and Measures*

Patients with SAUD did not differ from HC regarding general contrast discrimination involving unconstrained PC and MC activations from the FrACT ($W = 599.5$, $p = 0.351$) but did show lower visual acuity, $t(62.46) = 3.59$, $p < 0.001$. Weber contrast thresholds [mean (SD)] reached 1.96 (1.15) in patients with SAUD and 1.69 (0.70) in HC. Visual acuity [mean (SD)], measured in logMAR units[1], was 0.05 (0.12) in patients with SAUD and −0.05 (0.11) in HC. Mean visual acuity in both groups however remained within the range of normal vision (World Health Organization [WHO], 2019), arguing against functional visual loss in the SAUD group (Colenbrander, 2003)[2].

No group difference emerged on the steady ($W = 484$, $p = 0.434$) and pulsed-liked ($W = 493.5$, $p = 0.509$) attentional tasks, suggesting that group differences are not related to a higher rate of attentional lapses in SAUD. Mean (SD) percentage of correct responses of individuals with SAUD and HC, respectively, reached 98.6 (0.05) and 99.5 (0.01)% in the steady-like task and 99.3 (0.02) and 99.6 (0.01)% in the pulsed-like task.

**Table 2.** Post Hoc Comparisons of Interest Involving Group, Pedestal Condition, and Pedestal Luminance for Contrast Discrimination Thresholds Marginal Means and Slopes

| Contrast | Estimate | SE | Df | 95% CI | *t*-ratio | *p* |
|---|---|---|---|---|---|---|
| *Marginal means* | | | | | | |
| Pulsed – Steady in SAUD | 0.566 | 0.017 | 510 | [0.527; 0.605] | 32.61 | **<0.001** |
| Pulsed – Steady in HC | 0.592 | 0.017 | 510 | [0.553; 0.631] | 33.96 | **<0.001** |
| SAUD – HC for Steady | 0.078 | 0.029 | 63 | [0.011; 0.146] | 2.67 | **0.019** |
| SAUD – HC for Pulsed | 0.053 | 0.031 | 63 | [−0.017; 0.123] | 1.72 | 0.179 |
| *Slopes* | | | | | | |
| Pulsed – Steady in SAUD | 1.140 | 0.142 | 510 | [0.821; 1.460] | 8.03 | **<0.001** |
| Pulsed – Steady in HC | 0.745 | 0.142 | 510 | [0.426; 1.060] | 5.25 | **<0.001** |
| SAUD – HC for Steady | -0.003 | 0.116 | 510 | [−0.264; 0.257] | -0.03 | 1.000 |
| SAUD – HC for Pulsed | 0.392 | 0.164 | 510 | [0.024; 0.760] | 2.39 | **0.034** |

CI and *p*-values are Bonferroni-corrected. Df, degrees of freedom; HC, healthy controls; SAUD, severe alcohol use disorder; SE, standard error.

Alcohol-related indices (daily alcohol consumption, years of SAUD, duration of abstinence, number of previous detoxifications, AUDIT scores), daily tobacco use, education level, depression, state/trait anxiety, and benzodiazepine dosage did not correlate with patients' steady or pulsed pedestal thresholds and slopes (all $p$s $\geq 0.087$, see Appendix S3). We found no difference in thresholds and slopes between patients with SAUD still taking benzodiazepines and unmedicated patients on either the steady, thresholds: $t(95.59) = -0.02$, $p = 0.982$; slopes: $t(21.07) = 1.60$, $p = 0.124$, or pulsed, thresholds: $W = 1644$, $p = 0.637$; slopes: $t(16.26) = 0.183$, $p = 0.857$, pedestals.

With respect to smoking status, individuals with SAUD who smoked tobacco displayed lower steady pedestal thresholds (indicating better performance) than individuals with SAUD who did not, $t(83.88) = 2.67$, $p = 0.009$. A similar trend emerged for the pulsed pedestal, $t(57.95) = 1.96$, $p = 0.055$, suggesting that concurrent tobacco use did not potentiate visual deficits in individuals with SAUD (and thus did not favor group differences with HC). No such difference emerged for slopes, steady: $t(20.26) = -1.188$, $p = 0.249$; pulsed: $t(11.01) = -0.016$, $p = .987$.

## DISCUSSION

This study assessed potential PC/MC pathways alterations in SAUD and tested the hypothesis of selective MC deficits. We used a shortened version of the steady and pulsed psychophysical pedestal paradigms (Zhuang et al., 2012) and

[1]Negative values reflect higher (better) visual acuity.

[2]To investigate the potential influence of visual acuity further, we assessed its relationship with participants' raw contrast discrimination thresholds and slopes. We found that visual acuity only shared a moderate positive correlation with pulsed pedestal thresholds in individuals with SAUD ($r = .47$, $p = .006$). This result argues against a major link between participants' experimental scores and visual acuity, especially since this association may be theoretically explained by the PC dominance over acuity (Merigan et al., 1991), and the fact that contrast sensitivity at high spatial frequencies and acuity tap the same physiological bottleneck (Bach, 2007). Nevertheless, we examined whether including visual acuity in our LMM would help explaining participants' contrast discrimination thresholds by computing additional correlations between the residuals of our LMM and visual acuity scores. The absence of correlations in both individuals with SAUD ($r_s = .04$ $p = .446$) and HC ($r_s = .03$ $p = .605$) suggests that the variables included in the LMM already captured the linear relationship between visual acuity and contrast discrimination. Including acuity would therefore add redundant information and lead to a misspecified model owing to dependence. Being part of the SAUD group might be associated not only with lower contrast discrimination abilities but also with slight visual acuity changes, probably due to the tendency of patients to neglect ophthalmological care. As a result, they may present more untreated and hence uncorrected refractive errors compared to HC. However, only one individual with SAUD from our sample fell within the category of "mild distance vision impairment" (WHO, 2019) and excluding this participant did not modify the conclusions of our LMM. Together, these arguments thus do not support a major role of visual acuity in our results.

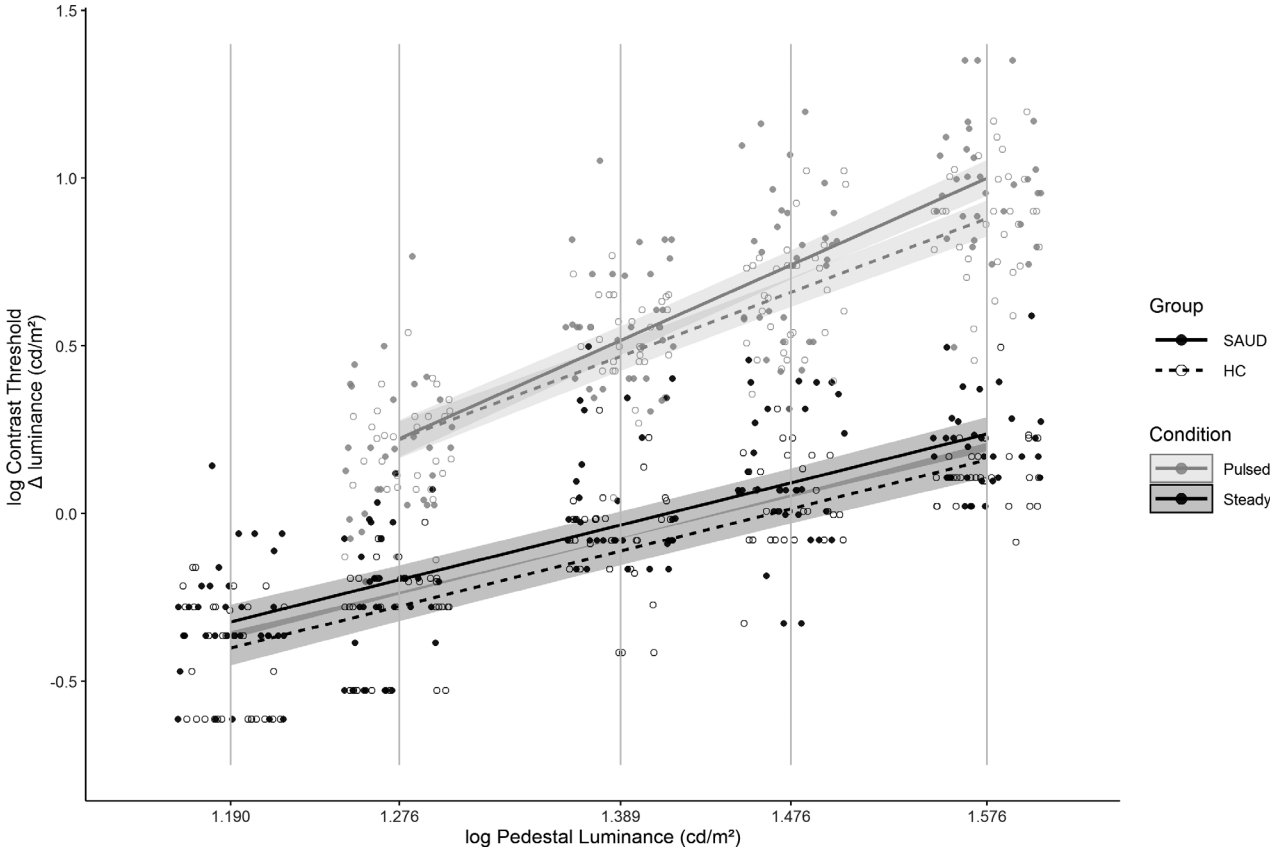


**Fig. 2.** Raw contrast discrimination thresholds of individuals with Severe Alcohol Use Disorders (SAUD) and healthy controls (HC) and Linear Mixed Model fit for the pulsed and steady pedestal conditions across the 5 fixed pedestal luminance values in each group (fixed effects only). Colored areas around the lines represent the 95% confidence intervals of each group mean in each condition. A small amount of random noise has been added to the location of the data points on the *x*-axis to show data dispersion and prevent overplotting.

compared the MC and PC-mediated contrast discrimination signatures of individuals with SAUD and HC in luminance increment conditions only.

Results showed the expected pattern of differentiation between pathways in HC, confirming that the experimental manipulation did work and ensuring reliable interpretation of group differences. In accordance with the theoretical framework sustaining the pulsed and pedestal paradigms (Pokorny and Smith, 1997), we observed higher contrast discrimination thresholds in the pulsed pedestal than in the steady one. Thresholds also followed the predicted monotonic increase with higher luminance values in the steady condition and escalated at a much steeper rate in the pulsed condition. We thus replicated the pattern of contrast discrimination of Zhuang et al. (2012) and efficiently triggered inferred MC and PC processing. Interestingly, individuals with SAUD demonstrated the same clear distinction between MC and PC-mediated contrast discrimination. This overall preservation of MC and PC functional properties, at least for luminance contrast, advocates against a massive loss of visual pathways specificity in SAUD. Actually, the general shape of contrast discrimination functions is supposed to mirror the properties of contrast gain mechanisms (i.e., how quickly cell responses increase with an increase in stimulus contrast, Kaplan and Shapley, 1986) originating at the retina level (Smith and Pokorny, 2003; Zele et al., 2010). As a result, our data argue against major retinal impairments in SAUD.

Beyond these qualitatively close contrast discrimination profiles across groups, our study revealed 2 main impairments among individuals with SAUD. First, they systematically presented higher contrast discrimination thresholds than HC in the steady condition. Regardless of the pedestal luminance level, they needed higher luminance differences, and hence higher contrasts, to detect the target squares. This finding reflects a loss of MC-mediated contrast sensitivity, probably due to poorer summation processes within the MC pathway. Indeed, compared with changes in shape, changes in the relative height of the contrast discrimination function are thought to reflect postretinal summation processes over populations of cells, probably at the cortical level (Pokorny and Smith, 1997; Zele et al., 2006, 2010). If the observed contrast sensitivity change was due to decrease quantum efficiency (i.e., reduced probability of getting a response when photons hit the retina) or phototransduction noise in photoreceptors, we would have noticed a similar influence on the PC pathway (Pokorny, 2011). The absence of parallel MC and PC decrease in contrast sensitivity points, therefore, toward changes at postreceptoral stages.

Second, individuals with SAUD displayed a higher slope than HC for the pulsed pedestal condition. This difference in slope suggests that there may be some subtle changes in PC-mediated contrast gain in SAUD, despite the abovementioned expected dissociations between MC and PC pathways. Response compression (i.e., shrinkage of available response amplitude) from a retinal or postretinal site, also observed in patients with optic neuritis (Cao et al., 2011), could produce the profile of PC contrast discrimination observed here. This profile is characterized by normal or near-normal discrimination near the adapting retinal luminance (i.e., the background luminance, 15.5 cd/m$^2$ or 1.19 log cd/m$^2$ in our study) but impaired discrimination for larger contrast steps from the adapting retinal luminance (Cao et al., 2011; Pokorny, 2011). While we did not directly evidence group differences in PC thresholds, Fig. 2 suggests that such differences could have emerged at higher pedestal luminance values (see Fig. 2). Then again, postretinal damage appears more plausible than retinal deficits as the latter would reduce ganglion cell firings rates per pedestal contrast step. This would result in fewer ganglion cell firing spikes for a normal threshold stimulus and lead, in fine, to a PC contrast discrimination slope flattening (Pokorny, 2011; Zele et al., 2010).

Our results thus provide only mixed evidence for the MC selective hypothesis. Even though we did observe a reduction in MC contrast sensitivity in SAUD, we also found modified PC contrast gain mechanisms. Our findings resemble those of Zhuang et al. (2012) who observed a selective reduction of MC contrast sensitivity and PC contrast gain under acute alcohol consumption. They are also consistent with reports of impaired contrast sensitivity for both low and high spatial frequencies in SAUD (da Cruz et al., 2016; Oliveira Castro et al., 2009; Roquelaure et al., 1995).

In line with results suggesting that the neurotoxicity of alcohol on the optic nerve could explain reduced contrast sensitivity in SAUD (Roquelaure et al., 1995; Zhuang et al., 2012), possibly through an increase of oxidative stress (Aviñó et al., 2002; Sancho-Tello et al., 2008), our study indicates potential postretinal impairments, limiting information transfer from the retina and LGN to the cortex, and/or degraded cortical processing of MC and PC signals. Damage to the optic nerve might also explain the prolonged latency and reduced amplitude of the P100 component frequently reported in studies exploring the visual evoked responses of individuals with SAUD (Chan et al., 1986; Cosi et al., 1986; Devetag, 1988). Blockage of conduction in the optic fibers responsible for central vision, including the papillo-macular bundles, could arise from nutritional deficiency and/or changes in neurotransmitter release or metabolism of cerebral amine caused by EtOH (Chan et al., 1986; Devetag, 1988). Either way, be the alterations subcortical or/and cortical, the absence of group differences in the attentional control tasks precludes a more general explanation in terms of reduced attentional resources rather than impoverished perceptual processing, confirming the presence of low-level visual deficits in SAUD. Importantly, these visual deficits could be persistent as reduced contrast sensitivity for Gabor patches at low spatial frequencies (0.5 and 0.8 cpd) has been documented in individuals with SAUD abstinent for more than 10 years (Martins et al., 2019). These changes, which mainly involve the MC pathway, were accompanied by color vision impairments, suggesting a combination of long-term MC and PC deficits that converge with our findings. Actually, PC-related color vision, which we did not explore in this study, might be more sensitive to the effects of low alcohol consumption dosage than luminance spatial contrast sensitivity as young adults with limited, nonproblematic, weekly habits of alcohol consumption have been found to exhibit signs of visual color impairment compared with age-matched control peers who do not drink, in the absence of any luminance contrast sensitivity changes (Brasil et al., 2015). Developmentally speaking, luminance contrast sensitivity changes, including MC-related alterations, might be more specifically linked to the chronicization and/or severity (frequency/dosage) of alcohol consumption.

From a clinical perspective, our results imply that more attention should be paid to SAUD patients' visual status as (i) subtle visual deficits may go unnoticed, and (ii) these visual disturbances might influence the successive cognitive processing stages, and notably disrupt predictive mechanisms critical for environmental adaptation and monitoring. Indeed, while visual alterations can hardly explain the onset of SAUD and directly account for all associated cognitive and emotional disturbances, visual and cognitive deficits could interact early on so that they should be considered simultaneously (Creupelandt et al., 2019). For that reason, the implications of this study must be appraised in relation to the early dynamics of human vision, and especially its coarse-to-fine tuning. If the quick but coarse MC analysis is not as efficient as expected, notably in terms of contrast processing which is useful to make objects distinguishable from the background or other objects, it will not efficiently inform the PC processing of fine details, leading to an overall poorer perception of visual stimuli. Besides, additional PC alterations would only add to this poorer guidance of vision and further impair critical processes such as recognition. The low-level sensory deficits identified in our study could thus exacerbate the well-established executive and emotional deficits of patients with SAUD. The present work promotes, therefore, the development of a theoretically integrated model of vision and cognition in SAUD, notably through studies testing the implications of impaired MC- and PC-related properties for cardinal features of SAUD such as attentional biases or emotional decoding (for a review and research agenda, see Creupelandt et al., 2019). Future studies are warranted to confirm the present results, further clarify their anatomic correlates, and investigate their influence on higher-order functions. In particular, even though the shape of the steady pedestal has been considered to reflect MC-mediated contrast gain in previous publications (e.g., Delord et al., 2006), it is recommended to use a third pedestal

paradigm—that is, the pedestal-Δ-pedestal task, of which the steady pedestal paradigm is the limiting case—to get a more generalizable measure of MC-mediated contrast gain. We did not use the pedestal-Δ-pedestal task to comply with previous visual contrast investigations in clinical populations (e.g., Delord et al., 2006; Greenaway et al., 2013) and to reduce the risk of low compliance and motivation as this task is considered as very difficult to perform even for healthy observers (Alexander et al., 2001). More precise measures of MC contrast are, therefore, warranted. At present, it also remains difficult to determine which alcohol consumption parameters may be most influential regarding visual changes. The lack of correlations between patients' performances and alcohol-related data might be partly explained by our limited SAUD sample size ($N = 33$) and the limited reliability of retrospective self-reported consumption measures (Del Boca et al., 2014). Whether tobacco use may moderate the influence of SAUD on PC and MC contrast processing will also have to be addressed in future dedicated studies.

In conclusion, individuals with SAUD demonstrated an overall preserved functional dissociation between MC and PC pathways but also displayed reduced MC-mediated contrast sensitivity and altered PC-mediated contrast gain. SAUD is thus associated with low-level perceptual deficits, which may originate (at least concerning contrast discrimination) at later stages of the retino-geniculo-striate pathway. These results stress the need to further study visual disturbances in SAUD, and their impact on cognitive deficits, to develop a more unified model of this condition.

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## CONFLICTS OF INTEREST

All of the authors reported no financial interests or potential conflict of interests.

## CONTRIBUTORS

All authors contributed to draft the study design. CC created the stimuli and programmed the task. CC, CL, and CG recruited the participants and collected the data. CC, FDH, and PM conducted the statistical analyses, and CC wrote the first draft of the manuscript. All authors provided critical revisions for important intellectual content and approved the final version of the manuscript.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Appendix S1.** Complementary analyses based on the original modeling equations of Pokorny and Smith (1997).

**Appendix S2.** Individual plots of participants' contrast discrimination thresholds.

**Appendix S3.** Correlations between psychophysical measures and alcohol-related, demographic and psychopathological variables in individuals with SAUD.