Supplementary Material

Rationale – ROI selection and relevance of the interaction GROUPxROI

To characterize the effects of ACHM on the cortical representation of the central visual field, we acquired fMRI data during visual stimulation, under photopic as well as scotopic luminance conditions, from ACHM participants and matched healthy controls (HC). Two fMRI data sets were collected and analysed independently: a conventional phase-encoded eccentricity mapping data set closely related to that used by Baseler et al.[31] and a state-of-the-art population receptive field (pRF) mapping data set following Dumoulin & Wandell[41]. For both data sets all fMRI measures were extracted from two regions of interest (ROI) in V1. These two ROIs were defined with an anatomically informed retinotopy atlas[53,54], thus splitting the representation surveyed with the visual stimuli (central 8°) into two 'anatomical bins' that are nominally equal in terms of the range of eccentricity they represent (0°-4° and 4°-8°). This way two ROIs were obtained, an ROI corresponding to the central visual field (0°-4°), termed $ROI_{central}$, and an ROI corresponding to the paracentral visual field (4°-8°), termed $ROI_{paracentral}$. To assess remapping effects associated with an absence of signalling from the rod-free fovea[31], we performed analyses comparing central and paracentral measures, i.e. $ROI_{central}$ and $ROI_{paracentral}$.

If remapping is characteristic of ACHM as a group, it would result in changes specifically in our measures from $ROI_{central}$. Here, we would expect a greater proportion of significant rod-driven visual responses and a representation of more peripheral eccentricities in ACHM than in controls. To address this, two-way mixed ANOVAs were applied separately for each luminance condition [factors GROUP (HC/ACHM) and ROI ($ROI_{central}$/$ROI_{paracentral}$)] and a response signature that indicates remapping of the central visual field representation would be reflected by a significant interaction of GROUPxROI, driven by effects in ACHM that are specific to $ROI_{central}$. Importantly, this approach ensures that main effects, e.g., generally reduced or enhanced responses in ACHM, are not mistaken for foveal remapping. At the same time, it offers a balance between sensitivity to the predicted effects and allowing for the fact that not all participants took part in all conditions.

Rationale – Relevance of mixed luminance comparison

It should be noted that neuro-computational model-based analysis approaches, such as pRF-mapping, have recently been reported to be vulnerable to an unanticipated lack of noise-cancellation and hence artefactual effects[81,82] such as the regression-to-the-mean[83]. In studies that compare pRF metrics between groups or conditions with differing signal-to-noise characteristics, apparent group/condition differences may actually be underpinned by effects of regression-to-the-mean. This is also relevant for comparisons between HC and patient data and has been addressed for ACHM by applying a "mixed luminance comparison", as described below.

In the present study fMRI responses were collected for both HC and ACHM under two luminance conditions, i.e., scotopic (primarily rod-driven) and photopic (in HC cone and rod-driven, in ACHM rod-driven). This prompts the question of which conditions are most informative for the group comparison to test for cortical remapping. Notably, in their pioneering study Baseler et al.[31] applied a comparison across different luminance conditions, here termed "mixed luminance comparison". They compared cortical responses in ACHM and HC for stimulation at different luminance levels in the two groups, i.e. photopic (7 cd/m^2) and scotopic luminance conditions (0.07 cd/m^2), respectively. The underlying rationale is as follows: Scotopic stimulation is normally needed to obtain purely rod-driven responses. Scotopic stimulation, however, creates reduced responses especially in ACHM, where responses are close to noise level in many participants. This might be due to reduced rod function in ACHM as reflected by ERG measurements[84–88]. However, in ACHM rod-driven responses can also be obtained for photopic stimulation as cone input is absent. Therefore, to assess the cortical representation of rod-only input in ACHM, the effect of noise in the rod-driven responses can be reduced by applying photopic stimulation in ACHM. In contrast, for HC rod-driven responses can only be isolated by applying scotopic stimulation. Hence a mixed luminance comparison, previously also applied in the ACHM study by Baseler et al.[31], is expected to reduce the effects of noise-contamination, such as regression-to-the-mean effects, in the data, which is particularly relevant for ACHM.

Phase-encoded eccentricity mapping of primary visual cortex (V1)

Averaged BOLD responses to the stimulus cycle

We visualized the averaged response to the stimulus cycle (Figure S2) and analysed this by calculating the discrete Fourier transform of each individual's mean time series to determine the differences in amplitudes obtained at the stimulation frequency (7 cycles/scan). Under photopic this condition this highlighted both an effect of GROUP (F (1, 31) = 14.64, p=.0006) and an interaction of GROUPxROI (F (1, 31) = 12.41, p=.0013). This can be taken as evidence for a central response dropout in one participant group and demonstrates that in the ACHM cohort the photopic responses reflect the typical features of the rod photoreceptor system. In contrast, under scotopic condition no group differences were evident (GROUP: F(1, 24) = 1.104, p=.3038; ROI: F(1, 24) = 3.666, p =.0675; GROUPxROI: F(1, 24) = 1.121; p=.3003). Importantly, the mixed luminance comparison (see Supplements under Rationale) only the factor ROI is significant (GROUP: F(1, 28) = 3.358, p=.078; ROI: F(1, 28) = 11.188, p = .002; GROUPxROI: F(1, 28) = 1.516; p=.228) which highlights already here the absence of foveal remapping as a group feature in ACHM.

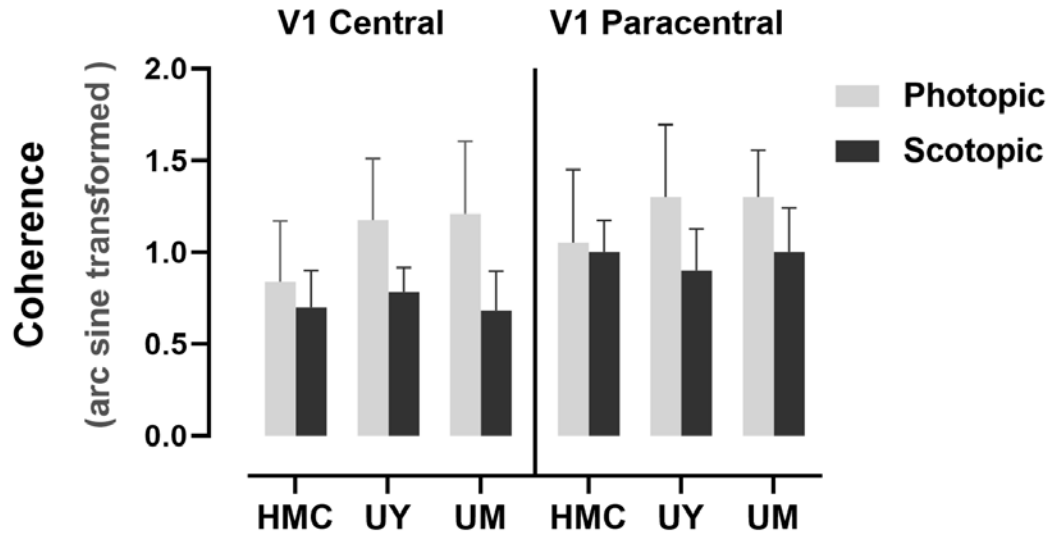

Figure S1

Reliability of fMRI signal across three different scanner sites. *Arc sine transformed coherence values are plotted for all participants in both regions of interest and across both viewing conditions; Whisker represents the SEM; n_{HMC} = 9, n_{UY} = 14, n_{UM} = 13)*

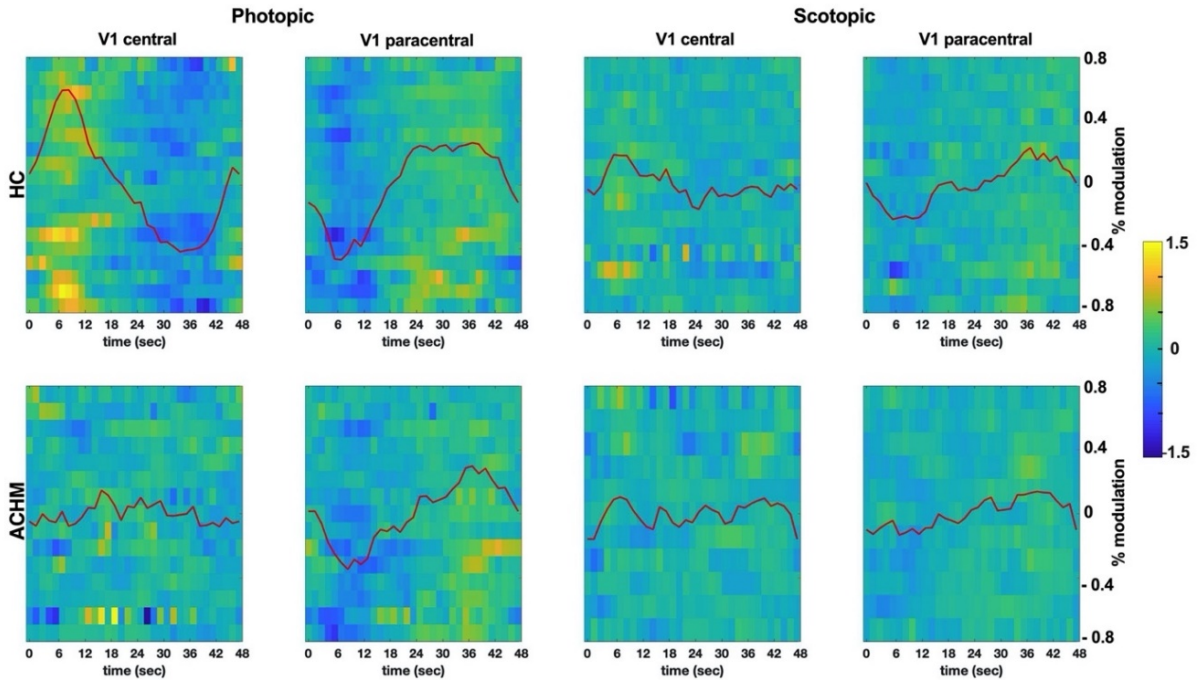

Figure S2

Percent modulation of responsive voxels in central and paracentral regions of interest in V1 averaged across stimulus cycles using conventional phase-encoded eccentricity mapping. *Top row: Single cycle averages in healthy control participants (HC) in the central and paracentral portion of V1 under two luminance levels; Bottom row: Single cycle averages in all ACHM participants for each ROI per luminance level. Each horizontal heat map line represents the averaged modulation in percent signal change of one participant; overlaid in black is the averaged modulation in percent signal change across all participants for each ROI; sample sizes:* N_{HC} *(photopic/scotopic) = 18/15;* N_{ACHM} *(photopic/scotopic) = 15/11*

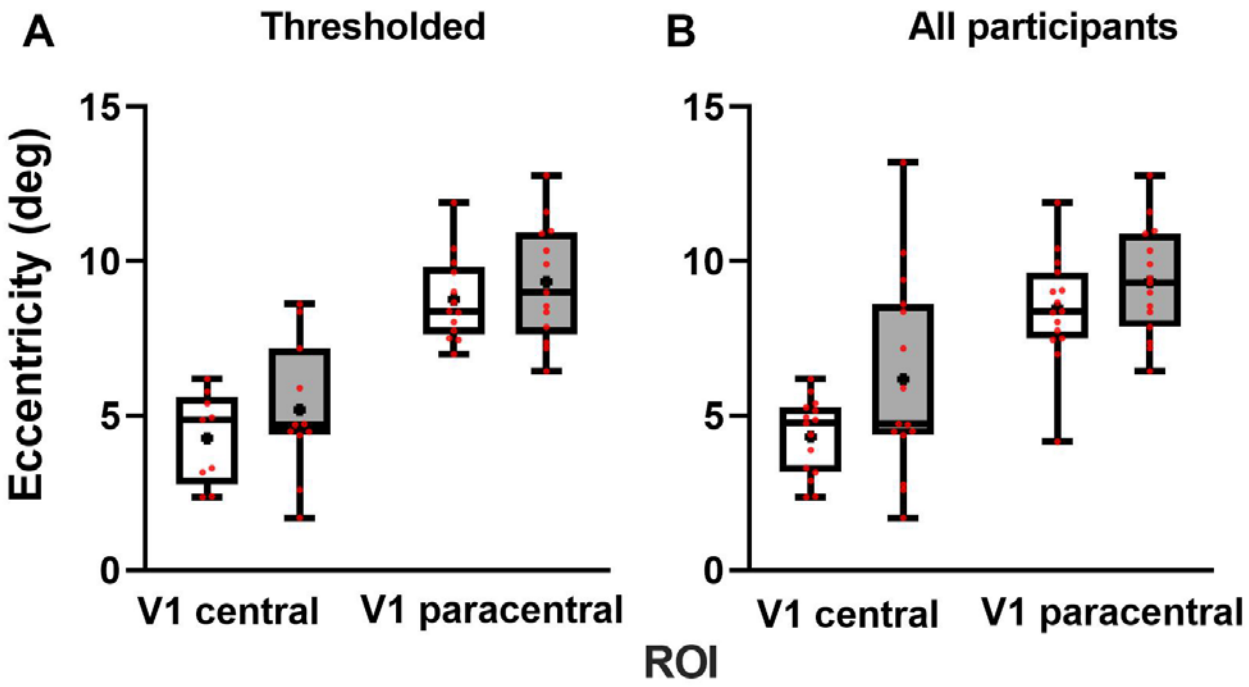

Figure S3

Population receptive field eccentricity estimates in central and paracentral portions of V1 in HC and ACHM participants*. Mean eccentricity (in degrees) of* $ROI_{central}$ *and* $ROI_{paracentral}$ *in V1 shown for both participant cohorts under the mixed condition. In (A) only participants above a 20% threshold of V1-proportion active were included while (B) depicts the standard sample as seen in Figure 3F. Whiskers present minimum and maximum values, while the box extends from the 25th to 75th percentiles. Median and mean are shown by a solid line and a +, respectively; individual data points are shown in red; sample size for thresholded condition:* N_{HC} *(central/paracentral) = 9/13;* N_{ACHM} *(central/paracentral) = 11/13.*

Fixed effects	**F (DFn, DFd)**	**P value**
Site	F (2, 32) = 0.27	0.7634
ROI	**F (1, 32) = 11.08**	**0.0022**
Luminance	**F (1, 32) = 23.37**	**<0.0001**
Site x ROI	F (2, 32) = 0.66	0.526
Site x Luminance	F (2, 32) = 1.20	0.3138
ROI x Luminance	F (1, 10) = 1.15	0.3096
Site x ROI x Luminance	F (2, 10) = 0.02	0.9789

Table S1
Linear mixed effects model results (REML) for fixed effects

Additional supplementary references

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