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MD Research News

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Drug treatment

Br J Ophthalmol. 2017 Jan;101(1):75-80. doi: 10.1136/bjophthalmol-2016-309313. Epub 2016 Dec 13.

The United Kingdom Diabetic Retinopathy Electronic Medical Record Users Group, Report 1: baseline characteristics and visual acuity outcomes in eyes treated with intravitreal injections of ranibizumab for diabetic macular oedema.

Egan C, Zhu H, Lee A, et al

AIMS: To describe baseline characteristics and visual outcome for eyes treated with ranibizumab for diabetic macular oedema (DMO) from a multicentre database.

METHODS: Structured clinical data were anonymised and extracted from an electronic medical record from 19 participating UK centres: age at first injection, ETDRS visual acuity (VA), number of injections, ETDRS diabetic retinopathy (DR) and maculopathy grade at baseline and visits. The main outcomes were change in mean VA from baseline, number of injections and clinic visits and characteristics affecting VA change and DR grade.

RESULTS: Data from 12 989 clinic visits was collated from baseline and follow-up for 3103 eyes. Mean age at first treatment was 66 years. Mean VA (letters) for eyes followed at least 2 years was 51.1 (SD=19.3) at baseline, 54.2 (SD: 18.6) and 52.5 (SD: 19.4) at 1 and 2 years, respectively. Mean visual gain was five letters. The proportion of eyes with VA of 72 letters or better was 25% (baseline) and 33% (1 year) for treatment naïve eyes. Eyes followed for at least 6 months received a mean of 3.3 injections over a mean of 6.9 outpatient visits in 1 year.

CONCLUSIONS: In a large cohort of eyes with DMO treated with ranibizumab injections in the UK, 33% of patients achieved better than or equal to 6/12 in the treated eye at 12 months compared with 25% at baseline. The mean visual gain was five letters. Eyes with excellent VA at baseline maintain good vision at 18 months.

PMID: 27965262

Cochrane Database Syst Rev. 2016 Dec 15;12:CD011160. [Epub ahead of print]

Anti-vascular endothelial growth factor for choroidal neovascularisation in people with pathological myopia.

Zhu Y, Zhang T, Xu G, Peng L.

BACKGROUND: Choroidal neovascularisation (CNV) is a common complication of pathological myopia. Once developed, most eyes with myopic CNV (mCNV) experience a progression to macular atrophy, which leads to irreversible vision loss. Anti-vascular endothelial growth factor (anti-VEGF) therapy is used to treat diseases characterised by neovascularisation and is increasingly used to treat mCNV.

OBJECTIVES: To assess the effects of anti-vascular endothelial growth factor (anti-VEGF) therapy for choroidal neovascularisation (CNV), compared with other treatments, sham treatment or no treatment, in people with pathological myopia.

SEARCH METHODS: We searched a number of electronic databases including CENTRAL and Ovid MEDLINE, ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform ICTRP). We did not use any date or language restrictions in the electronic searches for trials. Electronic databases were last searched on 16 June 2016.

SELECTION CRITERIA: We included randomised controlled trials (RCTs) and quasi-RCTs comparing anti-VEGF therapy with another treatment (e.g. photodynamic therapy (PDT) with verteporfin, laser photocoagulation, macular surgery, another anti-VEGF), sham treatment or no treatment in participants with mCNV.

DATA COLLECTION AND ANALYSIS: We used standard methodological procedures expected by Cochrane. Two authors independently screened records, extracted data, and assessed risk of bias. We contacted trial authors for additional data. We analysed outcomes as risk ratios (RRs) or mean differences (MDs). We graded the certainty of the evidence using GRADE.

MAIN RESULTS: The present review included six studies which provided data on the comparison between anti-VEGF with PDT, laser, sham treatment and another anti-VEGF treatment, with 594 participants with mCNV. Three trials compared bevacizumab or ranibizumab with PDT, one trial compared bevacizumab with laser, one trial compared aflibercept with sham treatment, and two trials compared bevacizumab with ranibizumab. Pharmaceutical companies conducted two trials. The trials were conducted at multiple clinical centres across three continents (Europe, Asia and North America). In all these six trials, one eye for each participant was included in the study. When compared with PDT, people treated with anti-VEGF agents (ranibizumab (one RCT), bevacizumab (two RCTs)), were more likely to regain vision. At one year of follow-up, the mean visual acuity (VA) in participants treated with anti-VEGFs was -0.14 logMAR better, equivalent of seven Early Treatment Diabetic Retinopathy Study (ETDRS) letters, compared with people treated with PDT (95% confidence interval (CI) -0.20 to -0.08, 3 RCTs, 263 people, low-certainty evidence). The RR for proportion of participants gaining 3+ lines of VA was 1.86 (95% CI 1.27 to 2.73, 2 RCTs, 226 people, moderate-certainty evidence). At two years, the mean VA in people treated with anti-VEGFs was -0.26 logMAR better, equivalent of 13 ETDRS letters, compared with people treated with PDT (95% CI -0.38 to -0.14, 2 RCTs, 92 people, low-certainty evidence). The RR for proportion of people gaining 3+ lines of VA at two years was 3.43 (95% CI 1.37 to 8.56, 2 RCTs, 92 people, low-certainty evidence). People treated with anti-VEGFs showed no obvious reduction (improvement) in central retinal thickness at one year compared with people treated with PDT (MD -17.84 µm, 95% CI -41.98 to 6.30, 2 RCTs, 226 people, moderate-certainty evidence). There was low-certainty evidence that people treated with anti-VEGF were more likely to have CNV angiographic closure at 1 year (RR 1.24, 95% CI 0.99 to 1.54, 2 RCTs, 208 people). One study allowed ranibizumab treatment as of month 3 in participants randomised to PDT, which may have led to an underestimate of the benefits of anti-VEGF treatment. When compared with laser photocoagulation, there was more improvement in VA among bevacizumab-treated people than among laser-treated people after one year (MD -0.22 logMAR, equivalent of 11 ETDRS letters, 95% CI -0.43 to -0.01, 1 RCT, 36 people, low-certainty evidence) and after two years (MD -0.29 logMAR, equivalent of 14 ETDRS letters, 95% CI -0.50 to -0.08, 1 RCT, 36 people, low-certainty evidence). When compared with sham treatment, people treated with aflibercept had better vision at one year (MD -0.19 logMAR, equivalent of 9 ETDRS letters, 95% CI -0.27 to -0.12, 1 RCT, 121 people, moderate-certainty evidence). The fact that this study allowed for aflibercept treatment at 6 months in the control group might cause an underestimation of the benefit with anti-VEGF. People treated with ranibizumab had similar improvement in VA recovery compared with people treated with bevacizumab after one year (MD -0.02 logMAR, equivalent of 1 ETDRS letter, 95% CI -0.11 to 0.06, 2 RCTs, 80 people, moderate-certainty evidence). Of the included six studies, two studies reported no adverse events in either group and two industry-sponsored studies reported both systemic and ocular adverse events. In the control group, there were no systemic or ocular adverse events reported in 149 participants. Fifteen people reported systemic serious adverse events among 359 people treated with anti-VEGF agents (15/359, 4.2%). Five people reported ocular adverse events among 359 people treated with anti-VEGF agents (5/359, 1.4%). The number of adverse events was low, and the estimate of RR was uncertain regarding systemic serious adverse events (4 RCTs, 15 events in 508 people, RR 4.50, 95% CI

0.60 to 33.99, very low-certainty evidence) and serious ocular adverse events (4 RCTs, 5 events in 508 people, RR 1.82, 95% CI 0.23 to 14.71, very low-certainty evidence). There were no reports of mortality or cases of endophthalmitis or retinal detachment. There was sparse reporting of data for vision-related quality of life (in favour of anti-VEGF) in only one trial at one year of follow-up. The studies did not report data for other outcomes, such as percentage of participants with newly developed chorioretinal atrophy.

AUTHORS' CONCLUSIONS: There is low to moderate-certainty evidence from RCTs for the efficacy of anti -VEGF agents to treat mCNV at one year and two years. Moderate-certainty evidence suggests ranibizumab and bevacizumab are equivalent in terms of efficacy. Adverse effects occurred rarely and the trials included here were underpowered to assess these. Future research should be focused on the efficacy and safety of different drugs and treatment regimens, the efficacy on different location of mCNV, as well as the effects on practice in the real world.

PMID: 27977064

Semin Ophthalmol. 2016 Dec 14:1-6. [Epub ahead of print]

Long-Term Outcomes in Patients with Neovascular Age-Related Macular Degeneration Who Maintain Dry Macula after Three Monthly Ranibizumab Injections.

Kim KM, Kim JH, Chang YS, Kim JW, Kim CG.

PURPOSE: To evaluate long-term changes in visual acuity and retinal microstructure in patients with neovascular age-related macular degeneration (AMD) who had maintained dry macula after initial treatment.

METHODS: This retrospective observational study included 55 eyes that were diagnosed with neovascular AMD, were treated with three monthly ranibizumab injections, and maintained dry macula during a two-year follow-up. Best-corrected visual acuity (BCVA) at three months and at the final follow-up were compared, and the degree of visual improvement was compared between eyes with and without improvement of the ellipsoid zone. In addition, the incidence of improvement of the ellipsoid zone was compared between eyes with different extents of disruption.

RESULTS: The mean follow-up period was 30.3 ± 4.1 months. BCVA at three months and at the final follow -up was 0.51 ± 0.46 and 0.45 ± 0.49 (P<0.001). Among 35 eyes that exhibited >200 μm of disruption of the ellipsoid zone, 15 (42.9%) showed improvement of the ellipsoid zone, and the improvement in BCVA was greater in these eyes than that in the remaining 20 eyes (P=0.021). A higher incidence of improvement of the ellipsoid zone was noted in eyes with 200 to 800 μm of disruption than in eyes with >800 μm of disruption (P<0.001).

CONCLUSIONS: Long-term improvement in visual acuity was noted in eyes that had maintained dry macula after three ranibizumab injections. The status of the ellipsoid zone at three months was closely associated with visual improvement.

PMID: 27960586

Graefes Arch Clin Exp Ophthalmol. 2016 Dec 12. [Epub ahead of print]

Vitreoretinal interface abnormalities in patients treated with ranibizumab for diabetic macular oedema.

Wong Y, Steel DH, Habib MS, Stubbing-Moore A, Bajwa D, Avery PJ; Sunderland Eye Infirmary study group.

PURPOSE: Intravitreal anti-vascular endothelial growth factor (VEGF) agents are effective in the treatment of central involving diabetic macular oedema (DMO). Vitreoretinal interface abnormalities (VRIA) are

common in patients with DMO, and the effect of these on the response to anti-VEGF treatment is unclear. Furthermore the effect of anti-VEGF agents on the VRIA itself is uncertain.

METHOD: Prospective study of consecutive patients treated with ranibizumab (RZB) for DMO as part of routine clinical care in one eye unit over a 1-year period. Visual acuity (Va), central retinal thickness (CRT) and injection frequency data was recorded on an electronic database. Treatment was initiated with four monthly RZB injections and then a monthly PRN regime. All patients underwent high-density spectral-domain optical coherence tomography (SDOCT) at baseline and 12 months. The SDOCTs were graded by two observers masked to the outcome.

RESULTS: One hundred and four eyes (77 patients) were included in the analysis. The mean age was 62 years, and 62% were male. The mean presenting vision was 62 letters and CRT 472 μm. Eighty eyes retained stable Va, and 17 had an improvement in Va. At baseline, 39 eyes had associated focal vitreomacular adhesion (VMA) and by 12 months this reduced to 30 ($p = 0.04$), with 12 releasing VMA and three developing it. Patients with VMA had significantly better final Va than those without VMA. Improvement in CRT was greatest in those where VMA released during the study. Forty-five eyes had some degree of foveal involving epiretinal membrane (ERM) at baseline, and 28 were considered to have clinically significant ERM. There was no clinically relevant change in ERM during the study. Patients with significant ERM at baseline had a lower final vision. Multivariate analysis showed that ERM and more severe retinopathy at baseline were predictive of less visual improvement ($p < 0.01$). Shorter intraretinal cyst length, ERM and the absence of VMA at baseline were predictive of a worsened anatomical response ($p < 0.001$).

CONCLUSION: VRIA are related to outcome in patients treated with RZB. ERM was associated with a worsened visual and anatomic response, and VMA with an improved anatomical response particularly when spontaneous VMA release occurred during treatment. The presence and severity of ERM was not affected by RZB treatment.

PMID: 27957600

Curr Pharm Des. 2016 Dec 16. [Epub ahead of print]

Hot topic in pharmacotherapy for neovascular age-related macular degeneration.

Falavarjani KG, Sadda SR.

BACKGROUND: The preferred approach for the treatment of neovascular age-related macular degeneration (AMD) is frequent intravitreal injections of the anti-vascular endothelial growth factor (VEGF) agents. However, considering the limitations of current anti-VEGF approaches, including the need for frequent injections, inadequate response in some patients, and a relatively short duration of effect, several new therapeutic modalities are under evaluation.

METHODS: A comprehensive review of the literature was performed on the new treatment modalities for neovascular AMD, and the relevant studies were discussed.

RESULTS: The treatment modalities for neovascular AMD include new anti-VEGF drugs, new drug delivery systems and new targets in the pathogenic cascade of choroidal neovascularization. These new modalities are in different phases of clinical development.

CONCLUSION: The results of the completed studies reporting the new therapeutic modalities for neovascular AMD thus far are promising.

PMID: 27981904

Sci Rep. 2016 Dec 14;6:39161.

Restoration of foveal photoreceptors after intravitreal ranibizumab injections for diabetic macular edema.

Mori Y, Suzuma K, Uji A, Ishihara K, Yoshitake S, Fujimoto M, Dodo Y, Yoshitake T, Miwa Y, Murakami T.

Abstract: Anti-vascular endothelial growth factor drugs are the first-line treatment for diabetic macular edema (DME), although the mechanism of the visual acuity (VA) improvement remains largely unknown. The association between photoreceptor damage and visual impairment encouraged us to retrospectively investigate the changes in the foveal photoreceptors in the external limiting membrane (ELM) and ellipsoid zone (EZ) on spectral-domain optical coherence tomography (SD-OCT) images in 62 eyes with DME treated with intravitreal ranibizumab (IVR) injections. The transverse lengths of the disrupted EZ and ELM were shortened significantly ($P < 0.001$ and $P = 0.044$, respectively) at 12 months. The qualitative investigation also showed restoration of the EZ and ELM lines on SD-OCT images. The EZ at 12 months lengthened in 34 of 38 eyes with discontinuous EZ and was preserved in 16 of 21 eyes with complete EZ at baseline. VA improvement was positively correlated with shortening of the disrupted EZ at 12 months ($\rho = 0.463$, $P < 0.001$), whereas the decrease in central subfield thickness was associated with neither VA improvement nor changes in EZ status ($\rho = 0.215$, $P = 0.093$ and ($\rho = 0.209$, $P = 0.103$, respectively). These data suggested that photoreceptor restoration contributes to VA improvement after pro re nata treatment with IVR injections for DME independent of resolved retinal thickening.

PMID: 27966644

Am J Ophthalmol. 2016 Dec 7. [Epub ahead of print]

Comparison of Time to Retreatment and Visual Function Between Ranibizumab and Aflibercept in Age-Related Macular Degeneration.

Maruyama-Inoue M, Yamane S, Sato S, Kadonosono K.

PMID: 27939299

Other treatment & diagnosis

Ophthalmic Surg Lasers Imaging Retina. 2016 Dec 1;47(12):1132-1136.

Photodynamic Therapy for Pseudophakic Eyes Compared to Eyes With Cataract.

Mimouni K, Mimouni M, Eldar I, Axer-Siegel R, Kramer M, Shani L, Weinberger D.

BACKGROUND AND OBJECTIVE: Verteporfin photodynamic therapy (vPDT) plays a role in the treatment of chorioretinal conditions. The purpose of this study was to compare vPDT outcomes between cataractous and pseudophakic eyes.

PATIENTS AND METHODS: In this prospective study of consecutive patients with choroidal neovascularization (CNV) secondary to neovascular age-related macular degeneration (nAMD) treated with vPDT, cataract and pseudophakic eyes were compared for number and timing of vPDT treatments, duration of follow-up, angiographic features, and changes in best-corrected visual acuity (BCVA).

RESULTS: Overall, 103 eyes (n = 95) were included in the final analysis; 44 eyes in the cataract group and 59 eyes in the pseudophakic group. No significant difference in change in BCVA ($P = .19$) or leakage-free CNV lesions ($P = .58$) was found between the groups.

CONCLUSIONS: In this study of vPDT for nAMD, there was no significant difference between eyes with cataract and pseudophakic eyes. It seems that cataract does not clinically alter the effect of vPDT.

PMID: 27977836

Ophthalmic Surg Lasers Imaging Retina. 2016 Dec 1;47(12):1106-1114.

Hyperreflective Choroidal Vessels in Geographic Atrophy Secondary to Age-Related Macular Degeneration.

Todisco L, Capuano V, Costanzo E, Recupero SM, Souied EH, Querques G.

BACKGROUND AND OBJECTIVE: To describe choroidal vessels in areas of geographic atrophy (GA) secondary to age-related macular degeneration that appear as hyperreflective choroidal vessels (HRCVs) on multicolor (MC) imaging.

PATIENTS AND METHODS: Retrospective case series of patients with GA. Multimodal imaging evaluation was performed.

RESULTS: HRCVs, which seem to be sclerotic on MC imaging, appeared as hyperautofluorescent on fundus autofluorescence, clearly distinguishable over the background of hypo-autofluorescence, and correlated with late-phase hypocyanescence areas on indocyanine green angiography. Average size of GA areas was significantly larger in eyes with (4.19 mm ± 0.83 mm) compared to eyes without (3.22 mm ± 1.05 mm) HRVCs (P = .0002). Similarly, mean choroidal thickness (CT) was significantly thinner in eyes with (78.5 µm ± 33.8 µm) compared to eyes without (155.4 µm ± 69.8 µm) HRVCs (P < .0001).

CONCLUSIONS: HRCVs are more clearly distinguishable than other choroidal vessels on MC imaging in GA. HRCV identification is more frequent in eyes with larger areas of atrophy and reduced CT, and thus possibly represent a maker of more advanced GA.

PMID: 27977833

Indian J Ophthalmol. 2016 Nov;64(11):829-834.

Pearl necklace sign in diabetic macular edema: Evaluation and significance.

Ajay K, Mason F, Gonglore B, Bhatnagar A.

PURPOSE: (1) The purpose of this study was to describe significance and prevalence of the newly reported pearl necklace spectral domain optical coherence tomography (SDOCT) sign, in diabetic macular edema (DMO), (2) to track the course of this sign over a period of at least 10 months.

MATERIALS AND METHODS: The pearl necklace SDOCT sign refers to hyperreflective dots in a contiguous ring around the inner wall of cystoid spaces in the retina, recently described for the first time in 21 eyes with chronic exudative maculopathy. A retrospective analysis was performed of SDOCT images of all patients presenting to the DMO referral clinic of a tertiary eye care center, over a period of 24 months. Images of patients displaying this sign were sequentially analyzed for at least 10 months to track the course of the sign.

RESULTS: Thirty-five eyes of 267 patients (13.1%) were found to display the pearl necklace sign. Twenty-eight eyes responded to intravitreal ranibizumab treatment with resolution of edema. In 21 eyes, the dots coalesced to form a clump, visible in the infrared fundus photograph as hard exudates; in seven eyes, dots disappeared without leaving visible exudates. In three eyes, the sign was seen in subfoveal cystoid spaces, with subsequent development of hard exudates, and drop in visual acuity of 20 letters or more.

CONCLUSION: Pearl necklace SDOCT sign is not infrequent in DMO. This sign is a precursor to hard exudates in the majority of cases. If this sign is seen subfoveally, drop in visual acuity can be expected, despite treatment.

PMID: 27958206

Am J Ophthalmol. 2016 Dec 13. [Epub ahead of print]

Retinal pigment epithelium degeneration associated with subretinal drusenoid deposits in age-related macular degeneration.

Xu X, Liu X, Wang X, Clark ME, McGwin G Jr, Owsley C, Curcio CA, Zhang Y.

PURPOSE: To test whether increased light transmission (hypertransmission) through subretinal drusenoid deposits (SDD) into the choroid in age-related macular degeneration (AMD) represented retinal pigment epithelium (RPE) degeneration.

DESIGN: Cross-sectional study.

METHODS: Nineteen eyes of 12 patients with early to intermediate stage AMD and 18 eyes of 12 normal subjects were evaluated with color fundus photography, optical coherence tomography (OCT), and high-resolution adaptive optics scanning laser ophthalmoscopy (AOSLO) at baseline and 24 months later. SDD were classified using an OCT-based 3-stage grading system. Hypertransmission beneath SDD into the choroid was examined in OCT. SDD microstructure was assessed with AOSLO. To characterize the hypertransmission associated chorioretinal degeneration, choroidal thickness and photoreceptor length were measured in OCT at 1 mm and 2 mm superior, inferior, temporal, and nasal to the foveal center.

RESULTS: OCT disclosed hypertransmission beneath stage 3 SDD in 8 eyes. These lesions showed a distinctive regressing structure in AOSLO, compared to stage 3 lesions without hypertransmission. The phenomenon persisted at follow-up, and new hypertransmission developed as SDD advanced. In eyes with hypertransmission, choroids were thinner than those of normal eyes at all sites (by 44-56%, $p \leq 0.0028$) and those of eyes with SDD but without hypertransmission at superior and temporal sites (by 31-46%, $p \leq 0.039$). Photoreceptors were significantly shorter than those in normal eyes (by 6-26%, $p \leq 0.0379$).

CONCLUSIONS: Hypertransmission into the choroid, accompanied with SDD regression and thinning of choroid and photoreceptor layers, indicates RPE degeneration associated with advanced stages in the SDD lifecycle.

PMID: 27986424

Retina. 2016 Dec 14. [Epub ahead of print]

GORE-TEX VASCULAR GRAFT FOR MACULAR BUCKLING IN HIGH MYOPIA EYES.

Wu PC, Sheu JJ, Chen YH, Chen YJ, Chen CH, Lee JJ, Huang CL, Chen CT, Kuo HK.

PURPOSE: To evaluate a new application of an expanded polytetrafluoroethylene (Gore-Tex) vascular graft for use in macular buckling surgery for treatment of highly myopic eyes.

METHODS: The Gore-Tex vascular graft was used as a macular buckling material in eight consecutive cases of myopic macular diseases which included fovea detachment, foveoschisis, or macular hole retinal detachment.

RESULTS: Retinal reattachment was achieved in all cases except one which had partial resolution (88%). The postoperative best-corrected visual acuity ranged from 20/2000 to 20/100 depending on the degree preexisting macular degeneration, and significant better than the preoperative best-corrected visual acuity ($P = 0.048$, paired t-test). During the follow-up period, which ranged from 8 months to 3 years, no eye developed buckle-related complications such as infection or dislocation.

CONCLUSION: The initial pilot results from this series using a Gore-Tex graft for macular buckling is promising. Throughout the follow-up period, the Gore-Tex was well tolerated in the highly myopic eyes. Large scale and long-term follow-up is warranted.

PMID: 27984549

Expert Opin Drug Deliv. 2016 Dec 14. [Epub ahead of print]

How are we improving the delivery to back of the eye? Advances and challenges of novel therapeutic approaches.

Agrahari V, Agrahari V, Mandal A, Pal D, Mitra AK.

INTRODUCTION: Drug delivery to the back of the eye requires strategic approaches that guarantee the long-term therapeutic effect with patient compliance. Current treatments for posterior eye diseases suffer from significant disadvantages including frequent intraocular injections of anti-VEGF agents and related adverse effects in addition to the high cost of the therapy. Areas covered: We summarize treatment challenges and promising drug delivery approaches for treatment of posterior segment eye diseases, such as age-related macular degeneration. Advances in the development of several nanotechnology-based systems, including stimuli-responsive approaches to enhance drug bioavailability and overcome existing barriers for effective ocular delivery are discussed. Stem cell transplantation and encapsulated cell technology approaches to treat posterior eye diseases are elaborated. Expert opinion: There are several drug delivery systems under development demonstrating promising results. However, a better understanding of ocular barriers, disease pathophysiology, and drug clearance mechanisms is required for better therapeutic outcomes. The stem cell transplantation strategy provides positive results in age-related macular degeneration therapy, but there are a number of challenges that must be overcome for long-term efficiency. Ultimately, there are numerous multidimensional challenges to cure vision problems and a collaborative approach among scientists is required.

PMID: 27967247

Pathogenesis

Neurochem Int. 2016 Oct 28. [Epub ahead of print]

A novel splice variant of the Excitatory Amino Acid Transporter 5: Cloning, immunolocalization and functional characterization of hEAAT5v in human retina.

Lee A, Stevens MG, Anderson AR, Kwan A, Balcar VJ, Pow DV.

Abstract: Excitatory Amino Acid Transporter 5 (EAAT5) is abundantly expressed by retinal photoreceptors and bipolar cells, where it acts as a slow glutamate transporter and a glutamate-gated chloride channel. The chloride conductance is large enough for EAAT5 to serve as an "inhibitory" glutamate receptor. Our recent work in rodents has shown that EAAT5 is differentially spliced and exists in many variant forms. The chief aim of the present study was to examine whether EAAT5 is also alternately spliced in human retina and, if so, what significance this might have for retinal function in health and disease. Retinal tissues from human donor eyes were used in RT-PCR to amplify the entire coding region of EAAT5. Amplicons of differing sizes were sub-cloned and analysis of sequenced data revealed the identification of wild-type human EAAT5 (hEAAT5) and an abundant alternately spliced form, referred to as hEAAT5v, where the open reading frame is expanded by insertion of an additional exon. hEAAT5v encodes a protein of 619 amino acids and when expressed in COS7 cells, the protein functioned as a glutamate transporter. We raised antibodies that selectively recognized the hEAAT5v protein and have performed immunocytochemistry to demonstrate expression in photoreceptors in human retina. We noted that in retinas afflicted by dry aged-related macular degeneration (AMD), there was a loss of hEAAT5v from the lesioned area and from photoreceptors adjacent to the lesion. We conclude that hEAAT5v protein expression may be perturbed in peri-lesional areas of AMD-afflicted retinas that do not otherwise exhibit evidence of damage. The loss of hEAAT5v could, therefore, represent an early pathological change in the development of AMD and might be involved in its aetiology.

PMID: 27984169

Adv Biosci Biotechnol. 2012;3:1167-1178.

Nitric oxide leads to cytoskeletal reorganization in the retinal pigment epithelium under oxidative stress.

Sripathi SR, He W, Um JY, Moser T, Dehnbostel S, Kindt K, Goldman J, Frost MC, Jahng WJ.

Abstract: Light is a risk factor for various eye diseases, including age-related macular degeneration (AMD) and retinitis pigmentosa (RP). We aim to understand how cytoskeletal proteins in the retinal pigment epithetlium (RPE) respond to oxidative stress, including light and how these responses affect apoptotic signaling. Previously, proteomic analysis revealed that the expression levels of vimentin and serine/ threonine protein phosphatase 2A (PP2A) are significantly increased when mice are exposed under continuous light for 7 days compared to a condition of 12 hrs light/dark cycling exposure using retina degeneration 1 (rd1) model. When melatonin is administered to animals while they are exposed to continuous light, the levels of vimentin and PP2A return to a normal level. Vimentin is a substrate of PP2A that directly binds to vimentin and dephosphorylates it. The current study shows that upregulation of PP2Ac (catalytic subunit) phosphorylation negatively correlates with vimentin phosphorylation under stress condition. Stabilization of vimentin appears to be achieved by decreased PP2Ac phosphorylation by nitric oxide induction. We tested our hypothesis that site-specific modifications of PP2Ac may drive cytoskeletal reorganization by vimentin dephosphorylation through nitric oxide signaling. We speculate that nitric oxide determines protein nitration under stress conditions. Our results demonstrate that PP2A and vimentin are modulated by nitric oxide as a key element involved in cytoskeletal signaling. The current study suggests that external stress enhances nitric oxide to regulate PP2Ac and vimentin phosphorylation, thereby stabilizing or destabilizing vimentin. Phosphorylation may result in depolymerization of vimentin, leading to nonfilamentous particle formation. We propose that a stabilized vimentin might act as an anti-apoptotic molecule when cells are under oxidative stress.

PMID: 27974994 PMCID: PMC5152770

Nat Rev Cardiol. 2016 Dec 15. [Epub ahead of print]

Long-term neprilysin inhibition - implications for ARNIs.

Campbell DJ.

Abstract: Neprilysin has a major role in both the generation and degradation of bioactive peptides. LCZ696 (valsartan/sacubitril, Entresto), the first of the new ARNI (dual-acting angiotensin-receptor-neprilysin inhibitor) drug class, contains equimolar amounts of valsartan, an angiotensin-receptor blocker, and sacubitril, a prodrug for the neprilysin inhibitor LBQ657. LCZ696 reduced blood pressure more than valsartan alone in patients with hypertension. In the PARADIGM-HF study, LCZ696 was superior to the angiotensin-converting enzyme inhibitor enalapril for the treatment of heart failure with reduced ejection fraction, and LCZ696 was approved by the FDA for this purpose in 2015. This approval was the first for chronic neprilysin inhibition. The many peptides metabolized by neprilysin suggest many potential consequences of chronic neprilysin inhibitor therapy, both beneficial and adverse. Moreover, LBQ657 might inhibit enzymes other than neprilysin. Chronic neprilysin inhibition might have an effect on angio-oedema, bronchial reactivity, inflammation, and cancer, and might predispose to polyneuropathy. Additionally, inhibition of neprilysin metabolism of amyloid-β peptides might have an effect on Alzheimer disease, age-related macular degeneration, and cerebral amyloid angiopathy. Much of the evidence for possible adverse consequences of chronic neprilysin inhibition comes from studies in animal models, and the relevance of this evidence to humans is unknown. This Review summarizes current knowledge of neprilysin function and possible consequences of chronic neprilysin inhibition that indicate a need for vigilance in the use of neprilysin inhibitor therapy.

PMID: 27974807

Front Immunol. 2016 Nov 28;7:542. eCollection 2016.

Complement Regulator FHR-3 Is Elevated either Locally or Systemically in a Selection of Autoimmune Diseases.

Schäfer N, Grosche A, Reinders J, Hauck SM, Pouw RB, Kuijpers TW, Wouters D, Ehrenstein B, Enzmann V, Zipfel PF, Skerka C, Pauly D.

Abstract: The human complement factor H-related protein-3 (FHR-3) is a soluble regulator of the complement system. Homozygous cfhr3/1 deletion is a genetic risk factor for the autoimmune form of atypical hemolytic-uremic syndrome (aHUS), while also found to be protective in age-related macular degeneration (AMD). The precise function of FHR-3 remains to be fully characterized. We generated four mouse monoclonal antibodies (mAbs) for FHR-3 (RETC) without cross-reactivity to the complement factor H (FH)-family. These antibodies detected FHR-3 from human serum with a mean concentration of 1 µg/mL. FHR-3 levels in patients were significantly increased in sera from systemic lupus erythematosus, rheumatoid arthritis, and polymyalgia rheumatica but remained almost unchanged in samples from AMD or aHUS patients. Moreover, by immunostaining of an aged human donor retina, we discovered a local FHR-3 production by microglia/macrophages. The mAb RETC-2 modulated FHR-3 binding to C3b but not the binding of FHR-3 to heparin. Interestingly, FHR-3 competed with FH for binding C3b and the mAb RETC-2 reduced the interaction of FHR-3 and C3b, resulting in increased FH binding. Our results unveil a previously unknown systemic involvement of FHR-3 in rheumatoid diseases and a putative local role of FHR-3 mediated by microglia/macrophages in the damaged retina. We conclude that the local FHR-3/FH equilibrium in AMD is a potential therapeutic target, which can be modulated by our specific mAb RETC-2.

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Lebecetin, a C-type lectin, inhibits choroidal and retinal neovascularization.

Montassar F, Darche M, Blaizot A, Augustin S, Conart JB, Millet A, Elayeb M, Sahel JA, Réaux-Le Goazigo A, Sennlaub F, Marrakchi N, Messadi E, Guillonneau X.

Abstract: Angiogenesis is a cause of visual impairment and blindness in the wet form of age-related macular degeneration and in ischemic retinopathies. Current therapies include use of anti-VEGF agents to reduce choroidal neovascularization (CNV) and edema. These treatments are effective in most cases, but spontaneous or acquired resistance to anti-VEGF and possible adverse effects of long-term VEGF inhibition in the retina and choroid highlight a need for additional alternative therapies. Integrins αvβ3 and αvβ5, which regulate endothelial cell proliferation and stabilization, have been implicated in ocular angiogenesis. Lebecetin (LCT) is a 30-kDa heterodimeric C-type lectin that is isolated from Macrovipera lebetina venom and interacts with α5β1- and αv-containing integrins. We previously showed that LCT inhibits human brain microvascular endothelial cell adhesion, migration, proliferation, and tubulogenesis. To evaluate the inhibitory effect of LCT on ocular angiogenesis, we cultured aortic and choroidal explants in the presence of LCT and analyzed the effect of LCT on CNV in the mouse CNV model and on retinal neovascularization in the oxygen-induced retinopathy model. Our data demonstrate that a single injection of LCT efficiently reduced CNV and retinal neovascularization in these models.

PMID: 27974593

J Biosci. 2016 Dec;41(4):667-676.

Expressions of visual pigments and synaptic proteins in neonatal chick retina exposed to light of variable photoperiods.

Jha KA, Nag TC, Wadhwa S, Roy TS.

Abstract: Light causes damage to the retina, which is one of the supposed factors for age-related macular degeneration in human. Some animal species show drastic retinal changes when exposed to intense light (e.g. albino rats). Although birds have a pigmented retina, few reports indicated its susceptibility to light damage. To know how light influences a cone-dominated retina (as is the case with human), we examined the effects of moderate light intensity on the retina of white Leghorn chicks (Gallus g. domesticus). The newly hatched chicks were initially acclimatized at 500 lux for 7 days in 12 h light: 12 h dark cycles (12L:12D). From posthatch day (PH) 8 until PH 30, they were exposed to 2000 lux at 12L:12D, 18L:6D (prolonged light) and 24L:0D (constant light) conditions. The retinas were processed for transmission electron microscopy and the level of expressions of rhodopsin, S- and L/M cone opsins, and synaptic proteins (Synaptophysin and PSD-95) were determined by immunohistochemistry and Western blotting. Rearing in 24L:0D condition caused disorganization of photoreceptor outer segments. Consequently, there were significantly decreased expressions of opsins and synaptic proteins, compared to those seen in 12L:12D and 18L:6D conditions. Also, there were ultrastructural changes in outer and inner plexiform layer (OPL, IPL) of the retinas exposed to 24L:0D condition. Our data indicate that the cone-dominated chick retina is affected in constant light condition, with changes (decreased) in opsin levels. Also, photoreceptor alterations lead to an overall decrease in synaptic protein expressions in OPL and IPL and death of degenerated axonal processes in IPL.

PMID: 27966487

Chin Med J (Engl). 2016 20th Dec;129(24):2944-2950.

Correlation of Vascular Endothelial Growth Factor Production with Photochemical Reaction-induced Retinal Edema.

Shan L, Zheng M, Zhang Y, Qu Y, Niu T, Gu Q, Liu K, Xia X.

BACKGROUND: Retinal edema is the major complication of retinal vein occlusion and diabetic retinopathy; it can damage visual function by influencing macular region. This study was to establish a rat retinal edema model and explore the related VEGF expression and observe the responses to anti-VEGF drugs in this model.

METHODS: A rat retinal edema model was established by inducing photochemical reaction using a 532 nm laser after the intravenous injection of Erythrosin B. Immediately after the laser treatment, models were given intravitreal injections of Ranibizumab or Conbercept to inhibit VEGF expression, and the changes of retinal thickness were measured. Retinal edema was observed using fundus photography (FP), optical coherence tomography (OCT), and fluoresce in fundus angiography (FFA) at 0, 1, 2, 4, 7 and 14 days after intervention. The retinal VEGF expression was measured using enzyme-linked immunosorbent assay (ELISA) and western blotting at each time point. The rat retinal edema model was also used to verify the function of anti-VEGF polypeptide ZY1.

RESULTS: Both retinal edema and vascular leakage were clearly observed at 1, 2 and 4 days after photochemical induction and the retinal thickness increased notably over the same period. The retinal VEGF expression peaked at day 1 and retina became thickening simultaneously. After the interventions, the VEGF expression of the Ranibizumab and Conbercept groups decreased at each time point compared to the edema group (26.90 ± 3.57 vs. 40.29 ± 6.68, $F = 31.269$ on day 1 and 22.36 ± 1.12 vs. 29.92 ± 0.93 $F = 163.789$ on day 2, both $P < 0.01$); the mean RT (278 ± 4 vs. 288 ± 3, $F = 134.190$ on day 1 and 274 ± 7 vs. 284 ± 6, $F = 64.367$ on day 2, both $P < 0.05$) and vascular leakage in these groups also decreased. The same results were observed in the ZY1 group, particularly at day 2 ($P < 0.05$).

CONCLUSIONS: This retinal edema model induced by a photochemical reaction is reliable and repeatable. Induced edema increases expression of VEGF. This model can be used to test new drugs.

PMID: 27958226

Cell Mol Life Sci. 2016 Dec 10. [Epub ahead of print]

Complement factor H in host defense and immune evasion.

Parente R, Clark SJ, Inforzato A, Day AJ.

Abstract: Complement is the major humoral component of the innate immune system. It recognizes pathogen- and damage-associated molecular patterns, and initiates the immune response in coordination with innate and adaptive immunity. When activated, the complement system unleashes powerful cytotoxic and inflammatory mechanisms, and thus its tight control is crucial to prevent damage to host tissues and allow restoration of immune homeostasis. Factor H is the major soluble inhibitor of complement, where its binding to self markers (i.e., particular glycan structures) prevents complement activation and amplification on host surfaces. Not surprisingly, mutations and polymorphisms that affect recognition of self by factor H are associated with diseases of complement dysregulation, such as age-related macular degeneration and atypical haemolytic uremic syndrome. In addition, pathogens (i.e., non-self) and cancer cells (i.e., altered-self) can hijack factor H to evade the immune response. Here we review recent (and not so recent) literature on the structure and function of factor H, including the emerging roles of this protein in the pathophysiology of infectious diseases and cancer.

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Epidemiology

Age Ageing. 2016 Dec 14. [Epub ahead of print]

Common eye diseases in older adults of southern Germany: results from the KORA-Age study.

Reitmeir P, Linkohr B, Heier M, Molnos S, Strobl R, Schulz H, Breier M, Faus T, Küster DM, Wulff A, Grallert H, Grill E, Peters A, Graw J.

PURPOSE: A population-based study in the region of Augsburg (Germany, KORA) was used to identify the prevalence of eye diseases and their risk factors in a sample of aged individuals.

METHODS: Data originated from the KORA-Age study collected in 2012 and 822 participants (49.6% women, 50.4% men, aged 68-96 years) were asked standardised questions about eye diseases. Positive answers were validated and specified by treating ophthalmologists. Additional information came from laboratory data. Polymorphic markers were tested for candidate genes.

RESULTS: We received validations and specifications for 339 participants. The most frequent eye diseases were cataracts (299 cases, 36%), dry eyes (120 cases, 15%), glaucoma (72 cases, 9%) and age-related macular degeneration (AMD) (68 cases, 8%). Almost all participants suffering from glaucoma or from AMD also had cataracts. Cataract surgery was associated with diabetes (in men; OR = 2.24; 95% confidence interval [CI] 1.11-4.53; P = 0.025) and smoking (in women; OR = 6.77; CI 1.62-28.35; P = 0.009). In men, treatments in airway diseases was associated with cataracts (glucocorticoids: OR = 5.29, CI 1.20-23.37; P = 0.028; sympathomimetics: OR = 4.57, CI 1.39-15.00; P = 0.012). Polymorphisms in two genes were associated with AMD (ARMS2: OR = 2.28, CI 1.48-3.51; P = 0.005; CFH: OR = 2.03, CI 1.35-3.06; P = 0.010).

CONCLUSION: Combinations of eye diseases were frequent at old age. The importance of classical risk factors like diabetes, hypertension and airway diseases decreased either due to a survivor bias leaving healthier survivors in the older age group, or due to an increased influence of other up to now unknown risk factors.

PMID: 27974306

Genetics

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Serum Levels of TIMP-3, LIPC, IER3 and SLC16A8 in CFH Negative AMD Cases.

Sharma K, Tyagi R, Singh R, Sharma SK, Anand A.

Abstract: AMD is a complex eye disease predominantly occurring in aged population. Till now about 53 genetic loci have been found to be associated with the AMD pathology. AMD pathogenesis is being increasingly known to progress through mechanisms independent of the CFH dependent pathway. Therefore, our aim for current study was to examine the genes by analyzing their expression levels in AMD. We recruited about 50 AMD and same number of age matched controls. We analysed the CFH duplication and deletion by multiplex ligation probe amplification (MLPA) and found no duplication and deletion in CFH gene in AMD patients. We also estimated the IER-3, SLC16A8, LIPC and TIMP-3 expression levels in both CFH negative AMD cases (i.e. no duplication and deletion in CFH gene) besides examining these in AMD and controls. We found that the expression level of LIPC, SLC16A8 and TIMP-3 was significantly associated with AMD pathology in both groups (LIPC: $p = 0.008$, SLC16A8: $p < 0.001$, TIMP-3: $p < 0.001$, respectively). However, we did not find any significant difference in IER-3 levels in AMD and controls. Therefore, the evidence from current study, suggests that AMD pathology may be mediated through mechanistic pathways linked to other genetic loci.

PMID: 27966779

Mol Immunol. 2016 Dec 6. [Epub ahead of print]

The complement system in age-related macular degeneration: A review of rare genetic variants and implications for personalized treatment.

Geerlings MJ, de Jong EK, den Hollander AI.

Abstract: Age-related macular degeneration (AMD) is a progressive retinal disease and the major cause of irreversible vision loss in the elderly. Numerous studies have found both common and rare genetic variants in the complement pathway to play a role in the pathogenesis of AMD. In this review we provide an overview of rare variants identified in AMD patients, and summarize the functional consequences of rare genetic variation in complement genes on the complement system. Finally, we discuss the relevance of this work in light of ongoing clinical trials that study the effectiveness of complement inhibitors against AMD.

PMID: 27939104

Annu Rev Pathol. 2016 Dec 5. [Epub ahead of print]

Complement Dysregulation and Disease: Insights from Contemporary Genetics.

Liszewski MK, Java A, Schramm EC, Atkinson JP.

Abstract: The vertebrate complement system consists of sequentially interacting proteins that provide for a rapid and powerful host defense. Nearly 60 proteins comprise three activation pathways (classical, alternative, and lectin) and a terminal cytolytic pathway common to all. Attesting to its potency, nearly half of the system's components are engaged in its regulation. An emerging theme over the past decade is that variations in these inhibitors predispose to two scourges of modern humans. One, occurring most often in childhood, is a rare but deadly thrombomicroangiopathy called atypical hemolytic uremic syndrome. The other, age-related macular degeneration, is the most common form of blindness in the elderly. Their seemingly unrelated clinical presentations and pathologies share the common theme of overactivity of the complement system's alternative pathway. This review summarizes insights gained from contemporary genetics for understanding how dysregulation of this powerful innate immune system leads to these human diseases.

PMID: 27959629

Stem cells

Cells. 2016 Dec 8;5(4). pii: E44.

Potential of Induced Pluripotent Stem Cells (iPSCs) for Treating Age-Related Macular Degeneration (AMD).

Fields M, Cai H, Gong J, Del Priore L.

Abstract: The field of stem cell biology has rapidly evolved in the last few decades. In the area of regenerative medicine, clinical applications using stem cells hold the potential to be a powerful tool in the treatment of a wide variety of diseases, in particular, disorders of the eye. Embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) are promising technologies that can potentially provide an unlimited source of cells for cell replacement therapy in the treatment of retinal degenerative disorders such as age-related macular degeneration (AMD), Stargardt disease, and other disorders. ESCs and iPSCs have been used to generate retinal pigment epithelium (RPE) cells and their functional behavior has been tested in vitro and in vivo in animal models. Additionally, iPSC-derived RPE cells provide an autologous source of cells for therapeutic use, as well as allow for novel approaches in disease modeling and drug development platforms. Clinical trials are currently testing the safety and efficacy of these cells in patients with AMD. In this review, the current status of iPSC disease modeling of AMD is discussed, as well as the challenges and potential of this technology as a viable option for cell replacement therapy in retinal degeneration.

PMID: 27941641

Diet, lifestyle and low vision

Acta Ophthalmol. 2016 Dec 14. [Epub ahead of print]

Homocysteine and risk of age-related macular degeneration: a systematic review and meta-analysis.

Pinna A, Zaccheddu F, Boscia F, Carru C, Solinas G.

Abstract: There is still no agreement on total plasma homocysteine (tHcy) role in age-related macular degeneration (AMD), the leading cause of new blindness in industrialized countries. We performed a systematic review and meta-analysis of the published data on the correlation between tHcy and AMD. MEDLINE/PubMed and ISI Web of Sciences searches were performed according to MOOSE guidelines. Case-control studies were eligible for inclusion. Participants and controls were AMD patients and subjects without AMD. The main outcome measure was wet AMD. Homocysteine level was the main exposure variable. Data were pooled using a random-effects model. Twelve case-control studies were identified: 10 assessed wet AMD, four dry AMD, one early AMD, one late AMD, and one any AMD. As for wet AMD, there was a total of 453 cases and 514 controls. Mean tHcy was on average 1.1 μmol/l (95% confidence interval [CI] = 0.96-1.25) greater in wet AMD cases, but there was evidence of extreme between-study heterogeneity ($p < 0.001$, $I2 = 91.8\%$). In a model homogenous for age, including six wet AMD studies (214 cases, 274 controls), mean tHcy was on average 0.58 μmol/l (95% CI = 0.35-0.73) greater in the case group, a not statistically significant result ($p = 0.144$) associated with moderate heterogeneity ($I2 = 39.2\%$). Our meta-analysis indicates that there is some weak evidence that increased tHcy might be associated with wet AMD; however, this result should be interpreted cautiously, because of a marked between-study heterogeneity and the possible effect of publication bias. Future studies, preferably of cohort design, are necessary before any firm conclusions on the putative role of increased tHcy on AMD can be drawn.

PMID: 27966830

Pharm Biol. 2017 Dec;55(1):571-580.

Photoprotective effects of cranberry juice and its various fractions against blue light-induced impairment in human retinal pigment epithelial cells.

Chang CH, Chiu HF, Han YC, Chen IH, Shen YC, Venkatakrishnan K, Wang CK.

CONTEXT: Cranberry has numerous biological activities, including antioxidation, anticancer, cardioprotection, as well as treatment of urinary tract infection (UTI), attributed to abundant phenolic contents.

OBJECTIVE: The current study focused on the effect of cranberry juice (CJ) on blue light exposed human retinal pigment epithelial (ARPE-19) cells which mimic age-related macular degeneration (AMD).

MATERIALS AND METHODS: Preliminary phytochemical and HPLC analysis, as well as total antioxidant capacity and scavenging activity of cranberry ethyl acetate extract and different CJ fractions (condensed tannins containing fraction), were evaluated. In cell line model, ARPE-19 were irradiated with blue light at 450 nm wavelength for 10 h (mimic AMD) and treated with different fractions of CJ extract at different doses (5-50 μg/mL) by assessing the cell viability or proliferation rate using MTT assay (repairing efficacy).

RESULTS: Phytochemical and HPLC analysis reveals the presence of several phenolic compounds (flavonoids, proanthocyanidin, quercetin) in ethyl acetate extract and different fractions of CJ. However, the condensed tannin containing fraction of ethyl acetate extract of CJ displayed the greater ($p < 0.05$) scavenging activity especially at the dose of 1 mg/mL. Similarly, the condensed tannin containing fraction at 50 μg/mL presented better ($p < 0.05$) repairing ability (increased cell viability). Furthermore, the oligomeric condensed tannin containing fraction display the best ($p < 0.05$) repairing efficiency at 50 μg/mL.

DISCUSSION AND CONCLUSION: In conclusion, this study distinctly proved that condensed tannin containing fraction of CJ probably exhibits better free radicals scavenging activity and thereby effectively protected the ARPE-19 cells and thus, hampers the progress of AMD.

PMID: 27937080

Arq Bras Oftalmol. 2016 Sep-Oct;79(5):323-327.

Repeatability of contrast sensitivity testing in patients with age-related macular degeneration, glaucoma, and cataract.

Kara S, Gencer B, Ersan I, Arikan S, Kocabiyik O, Tufan HA, Comez A.

PURPOSE: To analyze the intrasession and intersession repeatability of contrast sensitivity (CS) measurements in patients with glaucoma, cataract, or age-related macular degeneration (AMD) and healthy controls.

METHODS: CS measurements were performed using the OPTEC-Functional Vision Analyzer (FVA), which uses a standardized and closed (view-in) system. Measurements for patients with glaucoma, cataract, or AMD and healthy controls were repeated within 30 minutes (intrasession) and during two sessions (intersession), separated by one week to one month. Test-retest reliability and correlation were measured using the intraclass correlation coefficient (ICC) and coefficient of repeatability (COR).

RESULTS: Ninety subjects (90 eyes) with visual acuity of 0.17 logMAR or higher in the cataract group or 0.00 logMAR in the other groups were included. During the first session, the ICC values were 0.87, 0.90, 0.76, and 0.69, and COR values were 0.24, 0.20, 0.38, and 0.25 for the control, glaucoma, cataract, and AMD groups, respectively. The reliability scores significantly improved during the second session, except in the glaucoma group. There was an acceptable floor effect and no ceiling effect at higher frequencies in the glaucoma and AMD groups.

CONCLUSION: In subjects with good visual acuity, the FVA system is useful for evaluating CS and

demonstrates good repeatability, as shown by ICC and COR. Because there is no ceiling effect, this system is beneficial for evaluation of early changes in CS, particularly in patients with glaucoma or AMD.

PMID: 27982213

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Reversible Charles Bonnet Syndrome After Oculoplastic Procedures.

Beaulieu RA, Tamboli DA, Armstrong BK, Hogan RN, Mancini R.

Abstract: Individuals with Charles Bonnet syndrome (CBS) typically have severe visual loss and experience visual hallucinations yet have no psychiatric disease. Visual impairment often is due to end-stage glaucoma or macular degeneration. We report 3 cases of CBS in patients who underwent an oculoplastic surgical procedure. One patient experienced binocular visual distortion due to excessive topical ophthalmic ointment, and 2 patients experienced monocular visual impairment from patching. Visual hallucinations resolved once vision returned to baseline. We highlight the possibility of transient CBS in postoperative patients who have temporary iatrogenic vision impairment in one or both eyes.

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