Macular Disease Foundation AUSTRALIA
Our focus is your vision

MD Research News

Issue 195

Wednesday 27 August, 2014

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

If you have not already subscribed, please email Rob Cummins at **research@mdfoundation.com.au** with 'Subscribe to MD Research News' in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your 'unsubscribe' request.

Drug treatment

Br J Ophthalmol. 2014 Sep;98(9):1144-1167. doi: 10.1136/bjophthalmol-2014-305702.

Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA).

Schmidt-Erfurth U, Chong V, Loewenstein A, Larsen M, Souied E, Schlingemann R, Eldem B, Monés J, Richard G, Bandello F.

Abstract: Age-related macular degeneration (AMD) is still referred to as the leading cause of severe and irreversible visual loss world-wide. The disease has a profound effect on quality of life of affected individuals and represents a major socioeconomic challenge for societies due to the exponential increase in life expectancy and environmental risks. Advances in medical research have identified vascular endothelial growth factor (VEGF) as an important pathophysiological player in neovascular AMD and intraocular inhibition of VEGF as one of the most efficient therapies in medicine. The wide introduction of anti-VEGF therapy has led to an overwhelming improvement in the prognosis of patients affected by neovascular AMD, allowing recovery and maintenance of visual function in the vast majority of patients. However, the therapeutic benefit is accompanied by significant economic investments, unresolved medicolegal debates about the use of off-label substances and overwhelming problems in large population management. The burden of disease has turned into a burden of care with a dissociation of scientific advances and real-world clinical performance. Simultaneously, ground-breaking innovations in diagnostic technologies, such as optical coherence tomography, allows unprecedented high-resolution visualisation of disease morphology and provides a promising horizon for early disease detection and efficient therapeutic follow-up. However, definite conclusions from morphologic parameters are still lacking, and valid biomarkers have yet to be identified to provide a practical base for disease management. The European Society of Retina Specialists offers expert guidance for diagnostic and therapeutic management of neovascular AMD supporting healthcare givers and doctors in providing the best state-of-the-art care to their patients.

PMID: 25136079 [PubMed - as supplied by publisher]

Ophthalmol Ther. 2013 Dec;2(2):89-98. doi: 10.1007/s40123-013-0015-2. Epub 2013 Jun 25.

Aflibercept for the treatment of age-related macular degeneration.

Trichonas G, Kaiser PK.

Abstract: Aflibercept is a novel, recombinant, fusion protein that consists of portions of vascular endothelial

growth factor (VEGF) receptor (R) 1 and VEGFR2 extracellular domains fused to the Fc portion of human immunoglobulin G1. It exhibits higher affinity for VEGF-A/-B and binds all the VEGF isoforms (VEGF-B and -C, placental growth factor). The efficacy of aflibercept was assessed in two randomized, double-masked, multicenter, active-controlled, clinical trials in patients with choroidal neovascularization due to exudative age-related macular degeneration (AMD) and compared it's efficacy to ranibizumab, which is already Food and Drug Administration (FDA)-approved for patients with wet AMD. In the two trials known as VIEW 1 and VIEW 2, aflibercept was as effective when dosed as 2 mg every 8 weeks after 3 monthly loading doses compared to monthly ranibizumab. Aflibercept was well tolerated with very rare systemic adverse events, including arterial thromboembolic events (ATEs). The incidence of ATEs was 1.8% during the first year of the clinical trials and included non-fatal strokes, non-fatal myocardial infarction, or death from vascular events or an unknown cause. In November 2011, aflibercept received FDA approval and is currently used in clinical practice for patients with wet AMD.

PMID: 25135809 [PubMed] PMCID: PMC4108145

Graefes Arch Clin Exp Ophthalmol. 2014 Aug 22. [Epub ahead of print]

Bevacizumab and ranibizumab for neovascular age-related macular degeneration: an updated meta-analysis of randomised clinical trials.

Kodjikian L, Decullier E, Souied EH, Girmens JF, Durand EE, Chapuis FR, Huot L.

PURPOSE: Neovascular age-related macular degeneration (AMD) is the main cause of central vision loss among individuals aged 50 years or older in developed countries. The aim of this study was to review systematically the effect of bevacizumab compared to ranibizumab in patients with AMD at 1 year.

METHODS: A systematic review was performed on Medline, Embase, and the Cochrane Library and Trial registers to October 2013. Eligibility criteria for selecting studies were randomised controlled trials (RCT) comparing bevacizumab with ranibizumab in patients with neovascular AMD. Odds ratio (OR) and mean difference (MD) estimates were synthesized under fixed- and random-effects models. Heterogeneity was assessed using the Q statistic and I2.

RESULTS: Five RCTs were included, representing 2,686 randomised patients. The meta-analysis confirmed the non-inferiority of bevacizumab compared to ranibizumab for change in visual acuity at 1 year (MD 0.57 letters, -1.80 to 0.66, p = 0.37, I2 = 0 %). Better anatomical results were found for ranibizumab. Bevacizumab was associated with a 34 % increase in the number of patients with at least one serious systemic adverse event (OR 1.34, 1.08 to 1.66, p = 0.01, I2 = 0 %).

CONCLUSIONS: The pooled evidence confirmed that, compared with ranibizumab, bevacizumab was associated with equivalent effects on visual acuity at 1 year and with a higher risk of systemic serious adverse events. The current available data do not show which types of adverse events occur more frequently. In practice, bevacizumab should be used under a risk-management plan until further studies have been carried out to assess accurately the increased risk of systemic adverse events.

PMID: 25142373 [PubMed - as supplied by publisher]

Expert Opin Emerg Drugs. 2014 Aug 21:1-9. [Epub ahead of print]

Emerging drugs for diabetic macular edema.

Schwartz SG, Flynn HW Jr, Scott IU.

Introduction: Diabetic macular edema (DME) is the most common cause of visual impairment due to diabetic retinopathy. The treatment of DME has recently undergone a paradigm shift. Traditionally,

photocoagulation was standard treatment, but pharmacologic therapies are becoming increasingly used for this purpose. All currently available drug therapies for DME are either anti-VEGF agents or corticosteroids.

Areas covered: The pathogenesis of DME involves angiogenesis, inflammation and oxidative stress. The scientific rationale to treat DME through the pharmacologic blockade of VEGF and other pro-angiogenic factors is discussed. The fluocinolone insert is approved for the treatment of DME in several European countries, but not in the US at this time. Some medications that are already approved for other retinal diseases, most prominently aflibercept and the dexamethasone delivery system, have recently obtained approval for DME in the US. Other compounds are being studied in earlier-phase clinical trials.

Expert opinion: Pharmacologic treatment of DME will likely become increasingly used, especially for patients with edema involving the fovea. At this time, the two main classes of medication for treatment of DME are anti-VEGF agents and corticosteroids. As we continue to collect clinical trials data, the precise role of individual agents, and the continuing role for photocoagulation, will become more clear.

PMID: 25141904 [PubMed - as supplied by publisher]

PLoS One. 2014 Aug 21;9(8):e105280.

Deciphering Combinations of PI3K/AKT/mTOR Pathway Drugs Augmenting Anti-Angiogenic Efficacy In Vivo.

Sasore T, Kennedy B.

Abstract: Ocular neovascularization is a common pathology associated with human eye diseases e.g. age-related macular degeneration and proliferative diabetic retinopathy. Blindness represents one of the most feared disabilities and remains a major burden to health-care systems. Current approaches to treat ocular neovascularisation include laser photocoagulation, photodynamic therapy and anti-VEGF therapies: Ranibizumab (Lucentis) and Aflibercept (Eylea). However, high clinical costs, frequent intraocular injections, and increased risk of infections are challenges related with these standards of care. Thus, there is a clinical need to develop more effective drugs that overcome these challenges. Here, we focus on an alternative approach by quantifying the in vivo anti-angiogenic efficacy of combinations of phosphatidylinositol-3-kinase (PI3K) pathway inhibitors. The PI3K/AKT/mTOR pathway is a complex signalling pathway involved in crucial cellular functions such as cell proliferation, migration and angiogenesis. RT-PCR confirms the expression of PI3K target genes (pik3ca, pik3r1, mtor and akt1) in zebrafish trunks from 6 hours post fertilisation (hpf) and in eyes from 2 days post fertilisation (dpf). Using both the zebrafish intersegmental vessel and hyaloid vessel assays to measure the in vivo anti-angiogenic efficacy of PI3K/Akt/mTOR pathway inhibitors, we identified 5 µM combinations of i) NVP-BEZ235 (dual PI3K-mTOR inhibitor) + PI-103 (dual PI3K-mTOR inhibitor); or ii) LY-294002 (pan-PI3K inhibitor) + NVP-BEZ235; or iii) NVP-BEZ235 + rapamycin (mTOR inhibitor); or iv) LY-294002 + rapamycin as the most anti-angiogenic. Treatment of developing larvae from 2-5 dpf with 5 µM NVP-BEZ235 plus PI-103 resulted in an essentially intact ocular morphology and visual behaviour, whereas other combinations severely disrupted the developing retinal morphology and visual function. In human ARPE19 retinal pigment epithelium cells, however, no significant difference in cell number was observed following treatment with the inhibitor combinations. Collectively, these results highlight the potential of combinations of PI3K/AKT/mTOR pathway inhibitors to safely and effectively treat ocular neovascularization.

PMID: 25144531 [PubMed - in process]

Oman J Ophthalmol. 2014 May;7(2):104-6. doi: 10.4103/0974-620X.137178.

Retinal pigment epithelial tear after intravitreal bevacizumab injection for exudative age-related macular degeneration.

Singh SK, Deka S.

PMID: 25136244 [PubMed] PMCID: PMC4134543

Oman J Ophthalmol. 2014 May;7(2):78-80. doi: 10.4103/0974-620X.137162.

Long-term results of intravitreal ranibizumab for osteoma-related choroidal neovascularization in a child.

Gupta A, Gopal L, Sen P, Ratra D, Rao C.

Abstract: Though choroidal osteoma is a rare benign tumor, associated choroidal neovascularization (CNV) can be a cause of severe visual loss. A nine-year-old boy presented with one-month history of decreased vision in left eye. Upon a complete ophthalmologic examination, including fundus fluorescein angiography and optical coherence tomography, he was diagnosed with choroidal osteoma-related subfoveal CNV in the left eye. The CNV was associated with subretinal hemorrhage, subretinal fluid, and cystoid macular edema. Owing to the young age and subfoveal localization of the CNV, intravitreal ranibizumab injection was performed on this patient after a detailed discussion with the parents of its safety profile. No local or systemic complications were noted. No recurrence of CNV lesion was noted during 30 months of follow-up, and the vision was maintained. This report shows the favorable outcome of intravitreal injection of ranibizumab in choroidal osteoma-related CNV in a child.

PMID: 25136233 [PubMed] PMCID: PMC4134552

Br J Ophthalmol. 2014 Aug 19. pii: bjophthalmol-2014-305661. doi: 10.1136/bjophthalmol-2014-305661. [Epub ahead of print]

Sequential therapy with ranibizumab and dexamethasone intravitreal implant is better than dexamethasone monotherapy for macular oedema due to retinal vein occlusion.

Iu LP, Zhao P, Yeung IY, Fung NS, Lee JW, Wong RL, Chong V, Wong IY.

PURPOSE: To evaluate the efficacy and safety of sequential therapy with ranibizumab followed by dexamethasone intravitreal implant compared with dexamethasone monotherapy for macular oedema (MO) secondary to retinal vein occlusion (RVO).

METHODS: In this retrospective interventional study, the medical records of subjects with MO due to RVO who received either ranibizumab followed by dexamethasone intravitreal implant (Group 1) or dexamethasone-implant monotherapy (Group 2) were included. Primary outcome was the proportion of subjects who exhibited best-corrected visual acuity (VA) gain and resolution of MO within 6 months.

RESULTS: Thirty-three eyes were included (17 in Group 1, 16 in Group 2). More subjects in Group 1 exhibited a VA gain of at least 0.5 (LogMAR units hereafter) than Group 2 (29% vs 0%, p=0.044). The speed of VA gain was greater in Group 1 (1.4±0.8 months vs 2.7±1.4 months, p=0.020). MO was controlled in more subjects in Group 1 at all measured time intervals, and this difference was statistically significant at 3 months and 4 months. Subjects with branch RVO experienced VA gain more rapidly if they were from Group 1 (p=0.023).

CONCLUSIONS: Sequential therapy was found to be more effective than dexamethasone monotherapy in treating MO due to RVO.

PMID: 25138756 [PubMed - as supplied by publisher]

Other treatment and diagnosis

Klin Oczna. 2014;116(1):16-20.

[Increased expression of endothelin-1-- a novel diagnostic marker for early AMD detection?].[Article in Polish]

Machalińska A, Mozolewska-Piotrowska K, Paczkowska E, Lubiniski W.

AIM: The relationship between ischemic vascular disease and age-related macular degeneration may indicate the role of vascular injury as the primary insult causing functional deficits in age-related macular degeneration. The vasoactive factors produced by endothelial cells include endothelin-1 (ET-1), which is one of the most potent vasoconstricting peptides. In this study we sought to explore the potential role of endothelial dysfunction in the pathogenesis of age-related macular degeneration by measuring the concentration of ET-1 in peripheral blood of individuals diagnosed with age-related macular degeneration and evaluating its intracellular expression in peripheral blood cells, on mRNA level.

MATERIAL AND METHODS: Peripheral blood samples from 31 patients with diagnosed dry age-related macular degeneration and 46 patients with neovascular age-related macular degeneration were collected. Forty six age- and sex-matched volunteers without age-related macular degeneration were enrolled as a control group. ET-1 plasma levels were analyzed by ELISA and intracellular expression of ET-1 in peripheral blood cells was studied by using qRT-PCR.

RESULTS: The expression of intracellular ET-1 was significantly elevated in peripheral blood cells of both dry and wet age-related macular degeneration patients compared with the control subjects. Immunofluorescence staining revealed that ET-1 was specifically expressed in the circulating endothelial cells.

CONCLUSIONS: We assume that damaged endothelial cells may release a variety of vasoconstricting molecules, including ET-1, leading to derangement between the endothelium-derived relaxing and contracting factors. Local retinal ischemia consequently develops which may promote the development of retinal degeneration in patients with age-related macular degeneration,

PMID: 25137915 [PubMed - in process]

Pathogenesis

PLoS One. 2014 Aug 19;9(8):e105409. doi: 10.1371/journal.pone.0105409. eCollection 2014.

Complement factor h, vitronectin, and opticin are tyrosine-sulfated proteins of the retinal pigment epithelium.

Kanan Y, Siefert JC, Kinter M, Al-Ubaidi MR.

Abstract: Lack of tyrosine sulfation of ocular proteins results in disorganized photoreceptor structure and drastically reduced visual function, demonstrating the importance of this post-translational modification to vision. To understand the role that tyrosine sulfation plays in the function of ocular proteins, we identified some tyrosine-sulfated proteins in the retinal pigment epithelium using two independent methods, immuno-affinity column purification with an anti-sulfotyrosine specific antibody and computer-based sequence analysis of retinal pigment epithelium secretome by means of the prediction program Sulfinator. Radioactive labeling followed by thin layer electrophoresis revealed that three proteins, vitronectin, opticin, and complement factor H (CFH), were post-translationally modified by tyrosine sulfation. The identification of vitronectin and CFH as tyrosine-sulfated proteins is significant, since both are deposited in drusen in the eyes of patients with age-related macular degeneration (AMD). Furthermore, mutations in CFH have been determined to be a major risk factor in the development of AMD. Future studies that seek to understand the

role of CFH in the development of AMD should take into account the role that tyrosine sulfation plays in the interaction of this protein with its partners, and examine whether modulating sulfation provides a potential therapeutic target.

PMID: 25136834 [PubMed - in process] PMCID: PMC4138151

Expert Rev Clin Immunol. 2014 Aug 21:1-3. [Epub ahead of print]

IL-18: a new player in immunotherapy for age-related macular degeneration?

Campbell M, Doyle S, Humphries P.

Abstract: Recent evidence suggests that the pro-inflammatory cytokine IL-18 may have utility as an anti-angiogenic agent in the eye. Numerous laboratories, including our own have demonstrated the ability of murine IL-18 to prevent neovascularization in the retina, choroid and cornea in pathological scenarios. Here, we summarize the potential use of IL-18 as an immunotherapy for wet age-related macular degeneration treatment, describing past and recent findings pertaining to its biological function in the eye.

PMID: 25142147 [PubMed - as supplied by publisher]

J Endocrinol. 2014 Aug 20. pii: JOE-14-0349. [Epub ahead of print]

Oestrogen, ocular function and low-level vision: a review.

Hutchinson CV, Walker J, Davidson C.

Abstract: Over the last ten years, a literature has emerged concerning the sex steroid hormone oestrogen and its role in human vision. Here, we review evidence that oestrogen (estradiol) levels may significantly affect ocular function and low-level vision, particularly in older females. In doing so, we have examined a number of vision-related disorders including dry eye, cataract, increased intraocular pressure, glaucoma, age-related macular degeneration and Leber's hereditary optic neuropathy. In each case, we have found oestrogen, or lack thereof, to have a role. We have also included discussion of how oestrogen-related pharmacological treatments for menopause and breast cancer can impact the pathology of the eye and a number of psychophysical aspects of vision. Finally we have reviewed oestrogen's pharmacology and suggest potential mechanisms underlying its beneficial effects, with particular emphasis on anti-apoptotic and vascular effects.

PMID: 25143633 [PubMed - as supplied by publisher]

Front Aging Neurosci. 2014 Aug 1;6:191. doi: 10.3389/fnagi.2014.00191. eCollection 2014.

The generation of induced pluripotent stem cells for macular degeneration as a drug screening platform: identification of curcumin as a protective agent for retinal pigment epithelial cells against oxidative stress.

Chang YC, Chang WC, Hung KH, Yang DM, Cheng YH, Liao YW, Woung LC, Tsai CY, Hsu CC, Lin TC, Liu JH, Chiou SH, Peng CH, Chen SJ.

Abstract: Age-related macular degeneration (AMD) is one retinal aging process that may lead to irreversible vision loss in the elderly. Its pathogenesis remains unclear, but oxidative stress inducing retinal pigment epithelial (RPE) cells damage is perhaps responsible for the aging sequence of retina and may play an important role in macular degeneration. In this study, we have reprogrammed T cells from patients with dry type AMD into induced pluripotent stem cells (iPSCs) via integration-free episomal vectors and

differentiated them into RPE cells that were used as an expandable platform for investigating pathogenesis of the AMD and in-vitro drug screening. These patient-derived RPEs with the AMD-associated background (AMD-RPEs) exhibited reduced antioxidant ability, compared with normal RPE cells. Among several screened candidate drugs, curcumin caused most significant reduction of ROS in AMD-RPEs. Pre-treatment of curcumin protected these AMD-RPEs from H2O2-induced cell death and also increased the cytoprotective effect against the oxidative stress of H2O2 through the reduction of ROS levels. In addition, curcumin with its versatile activities modulated the expression of many oxidative stress-regulating genes such as PDGF, VEGF, IGFBP-2, HO1, SOD2, and GPX1. Our findings indicated that the RPE cells derived from AMD patients have decreased antioxidative defense, making RPE cells more susceptible to oxidative damage and thereby leading to AMD formation. Curcumin represented an ideal drug that can effectively restore the neuronal functions in AMD patient-derived RPE cells, rendering this drug an effective option for macular degeneration therapy and an agent against aging-associated oxidative stress.

PMID: 25136316 [PubMed] PMCID: PMC4117985

J Ophthalmol. 2014;2014:530943. doi: 10.1155/2014/530943. Epub 2014 Jul 14.

The Mitochondria-Targeted Antioxidant SkQ1 Downregulates Aryl Hydrocarbon Receptor-Dependent Genes in the Retina of OXYS Rats with AMD-Like Retinopathy.

Perepechaeva ML, Grishanova AY, Rudnitskaya EA, Kolosova NG.

Abstract: The mitochondria-targeted antioxidant SkQ1 is a novel drug thought to retard development of age -related diseases. It has been shown that SkQ1 reduces clinical signs of retinopathy in senescence-accelerated OXYS rats, which are a known animal model of human age-related macular degeneration (AMD). The aim of this work was to test whether SkQ1 affects transcriptional activity of AhR (aryl hydrocarbon receptor) and Nrf2 (nuclear factor erythroid 2-related factor 2), which are considered as AMD-associated genes in the retina of OXYS and Wistar rats. Our results showed that only AhR and AhR-dependent genes were sensitive to SkQ1. Dietary supplementation with SkQ1 decreased the AhR mRNA level in both OXYS and Wistar rats. At baseline, the retinal Cyp1a1 mRNA level was lower in OXYS rats. SkQ1 supplementation decreased the Cyp1a1 mRNA level in Wistar rats, but this level remained unchanged in OXYS rats. Baseline Cyp1a2 and Cyp1b1 mRNA expression was stronger in OXYS than in Wistar rats. In the OXYS strain, Cyp1a2 and Cyp1b1 mRNA levels decreased as a result of SkQ1 supplementation. These data suggest that the Cyp1a2 and Cyp1b1 enzymes are involved in the pathogenesis of AMD-like retinopathy of OXYS rats and are possible therapeutic targets of SkQ1.

PMID: 25132985 [PubMed] PMCID: PMC4123489

Proc Natl Acad Sci U S A. 2014 Aug 19. pii: 201324235. [Epub ahead of print]

Endothelial cell FGF signaling is required for injury response but not for vascular homeostasis.

Oladipupo SS, Smith C, Santeford A, Park C, Sene A, Wiley LA, Osei-Owusu P, Hsu J, Zapata N, Liu F, Nakamura R, Lavine KJ, Blumer KJ, Choi K, Apte RS, Ornitz DM.

Abstract: Endothelial cells (ECs) express fibroblast growth factor receptors (FGFRs) and are exquisitely sensitive to FGF signals. However, whether the EC or another vascular cell type requires FGF signaling during development, homeostasis, and response to injury is not known. Here, we show that Flk1-Cre or Tie2-Cre mediated deletion of FGFR1 and FGFR2 (Fgfr1/2Flk1-Cre or Fgfr1/2Tie2-Cre mice), which results in deletion in endothelial and hematopoietic cells, is compatible with normal embryonic development. As adults, Fgfr1/2Flk1-Cre mice maintain normal blood pressure and vascular reactivity and integrity under homeostatic conditions. However, neovascularization after skin or eye injury was significantly impaired in

both Fgfr1/2Flk1-Cre and Fgfr1/2Tie2-Cre mice, independent of either hematopoietic cell loss of FGFR1/2 or vascular endothelial growth factor receptor 2 (Vegfr2) haploinsufficiency. Also, impaired neovascularization was associated with delayed cutaneous wound healing. These findings reveal a key requirement for cell-autonomous EC FGFR signaling in injury-induced angiogenesis, but not for vascular homeostasis, identifying the EC FGFR signaling pathway as a target for diseases associated with aberrant vascular proliferation, such as age-related macular degeneration, and for modulating wound healing without the potential toxicity associated with direct manipulation of systemic FGF or VEGF activity.

PMID: 25139991 [PubMed - as supplied by publisher]

Diet & lifestyle

Oxid Med Cell Longev. 2014;2014:671539. Epub 2014 Jul 20.

The Protective Role of Antioxidants in the Defence against ROS/RNS-Mediated Environmental Pollution.

Poljšak B, Fink R.

Abstract: Overproduction of reactive oxygen and nitrogen species can result from exposure to environmental pollutants, such as ionising and nonionising radiation, ultraviolet radiation, elevated concentrations of ozone, nitrogen oxides, sulphur dioxide, cigarette smoke, asbestos, particulate matter, pesticides, dioxins and furans, polycyclic aromatic hydrocarbons, and many other compounds present in the environment. It appears that increased oxidative/nitrosative stress is often neglected mechanism by which environmental pollutants affect human health. Oxidation of and oxidative damage to cellular components and biomolecules have been suggested to be involved in the aetiology of several chronic diseases, including cancer, cardiovascular disease, cataracts, age-related macular degeneration, and aging. Several studies have demonstrated that the human body can alleviate oxidative stress using exogenous antioxidants. However, not all dietary antioxidant supplements display protective effects, for example, β-carotene for lung cancer prevention in smokers or tocopherols for photooxidative stress. In this review, we explore the increases in oxidative stress caused by exposure to environmental pollutants and the protective effects of antioxidants.

PMID: 25140198 [PubMed - as supplied by publisher] PMCID: PMC4129148

Br J Ophthalmol. 2014 Aug 19. pii: bjophthalmol-2014-305324.

A comparison of methods used to evaluate mobility performance in the visually impaired.

Warrian KJ, Katz LJ, Myers JS, Moster MR, Pro MJ, Wizov SS, Spaeth GL.

PURPOSE: To compare three different approaches to measuring mobility performance when evaluating the visually impaired.

METHODS: 488 participants, including 192 glaucoma, 112 age-related macular degeneration, 91 diabetic retinopathy and 93 healthy volunteers, completed the Assessment of Disability Related to Vision (ADREV) mobility course. The performance of participants on the mobility course was evaluated by noting errors made and time required for completion. Errors noted and time taken were compared using multivariate logistic regression to determine which measurement better differentiated patients with visual disease from healthy volunteers. Multivariate logistic regression was also used to evaluate the combined metric of ADREV errors divided by time to determine its ability to discriminate participants with visual disease from healthy volunteers.

RESULTS: Errors noted and time taken while ambulating through the standardised mobility course shared

a weak but statistically significant association (Pearson's r=0.36, p<0.05). After controlling for demographic and medical comorbidities, logistic regression analysis revealed that errors noted were better at discriminating individuals with visual disease from healthy volunteers (OR 2.8-4.9, 95% CI 1.5 to 10.3) compared with the time taken for mobility course completion (OR 1.1, 95% CI 1.0 to 1.2). These findings were consistent across all comparisons between healthy volunteers and participants with each type of visual impairment. Finally, the combined metric of ADREV errors divided by time was far more predictive of visual disease compared with either time taken or errors noted during mobility testing (OR 11.0-17.7, 95% CI 3.6 to 77.1).

CONCLUSIONS: A validated scoring system based on errors is more effective when assessing visual disability during mobility testing than recording the time taken for course completion. The combined metric of ADREV errors noted divided by time taken was most predictive of all the methods used to evaluate visual disability during mobility testing.

PMID: 25138757 [PubMed - as supplied by publisher]

Ophthalmol Ther. 2014 Mar 29. [Epub ahead of print]

Antioxidants Improve the Viability of Stored Adult Retinal Pigment Epithelial-19 Cultures.

Pasovic L, Eidet JR, Lyberg T, Messelt EB, Aabel P, Utheim TP.

INTRODUCTION: There is increasing evidence that retinal pigment epithelium (RPE) can be used to treat age-related macular degeneration, one of the leading causes of blindness worldwide. However, the best way to store RPE to enable worldwide distribution is unknown. We investigated the effects of supplementing our previously published storage method with seven additives, attempting to improve the number of viable adult retinal pigment epithelial (ARPE)-19 cells after storage.

MATERIALS AND METHODS: ARPE-19 cells were cultured on multiwell plates before being stored for 1 week at 16 °C. Unsupplemented Minimal Essential Medium (MEM) (control) and a total of seven individual additives (DADLE ([D-Ala2, D-Leu5]-encephalin), capsazepine, docosahexaenoic acid (DHA), resveratrol, quercetin, simvastatin and sulforaphane) at three to four concentrations in MEM were tested. The individual effect of each additive on cell viability was analyzed with a microplate fluorometer. Cell phenotype was investigated by both microplate fluorometer and epifluorescence microscopy, and morphology by scanning electron microscopy.

RESULTS: Supplementation of the storage medium with DADLE, capsazepine, DHA or resveratrol significantly increased the number of viable cells by 86.1% ± 41.9%, 67.9% ± 24.7%, 36.5% ± 10.3% and 21.1% ± 6.4%, respectively, compared to cells stored in unsupplemented MEM. DHA and resveratrol significantly reduced caspase-3 expression, while expression of RPE65 was maintained across groups.

CONCLUSION: The number of viable ARPE-19 cells can be increased by the addition of DADLE, capsazepine, DHA or resveratrol to the storage medium without perturbing apoptosis or differentiation.

PMID: 25134496 [PubMed - as supplied by publisher]

Curr Genomics. 2014 Aug;15(4):266-77. doi: 10.2174/1389202915666140516204512.

Using current data to define new approach in age related macular degeneration: need to accelerate translational research.

Anand A, Sharma K, Chen W, Sharma NK.

Abstract: Age related macular degeneration (AMD) is one of the major retinal degenerative disease of ageing whose complex genetic basis remains undeciphered. The involvement of various other factors like

mitochondrial genes, cytoskeletal proteins and the role of epigenetics has been described in this review. Several population based AMD genetic studies have been carried out worldwide. Despite the increased publication of reports, clinical translation still eludes this davastating disease. We suggest models to address roadblocks in clinical translation hoping that these would be beneficial to drive AMD research towards innovative biomarkers and therapeutics Therefore, addressing the need large autopsy studies and combining it with efficient use of bioinformatic tools, statistical modeling and probing SNP-biomarker association are key to time bound resolution of this disease.

PMID: 25132797 [PubMed] PMCID: PMC4133950