- 1 Title:THE POTENTIAL AND VALUE OF OBJECTIVE EYE TRACKING IN THE
- 2 OPHTHALMOLOGY CLINIC

3

## 4 Authors

- 5 Rosie Clark, Population Health Sciences, Bristol Medical School, Bristol University,
- 6 Bristol, UK
- 7 James Blundell, Institute of Future Transport and Cities, Coventry University, UK
- 8 Matt J Dunn, School of Optometry and Vision Sciences, Cardiff University, Cardiff,
- 9 UK
- Jonathan T Erichsen, School of Optometry and Vision Sciences, Cardiff University,
- 11 Cardiff, UK
- Mario E Giardini, Department of Biomedical Engineering, University of Strathclyde,
- 13 Glasgow, UK
- 14 Irene Gottlob, Department of Neuroscience, Psychology & Behaviour, University of
- 15 Leicester, Leicester, UK
- 16 Chris Harris, School of Psychology Plymouth University, UK & Royal Eye Infirmary,
- 17 Derriford Hospital, Plymouth UK
- 18 Helena Lee, Clinical and Experimental Sciences, University of Southampton, UK
- 19 Lee Mcilreavy, School of Optometry and Vision Sciences, Cardiff University,
- 20 Cardiff, UK
- 21 Andrew Olson, School of Psychology, University of Birmingham, Birmingham, UK

22 Jay E Self, Clinical and Experimental Sciences, University of Southampton. UK Valldeflors Vinuela-Navarro, Ophthalmic Research Group, Life and Health 23 24 Sciences, Aston University, UK Jonathan Waddington, Research and Development, WESC Foundation, Exeter, UK 25 J Margaret Woodhouse, School of Optometry and Vision Sciences, Cardiff 26 27 University, Cardiff, UK lain D Gilchrist, School of Psychological Science, Bristol University, Bristol, UK 28 Cathy Williams, Population Health Sciences, Bristol Medical School, Bristol 29 University, Bristol, UK 30 31 32 Correspondence to: 33 Cathy Williams, Population Health Sciences, Bristol Medical School, Bristol 1-5 Whiteladies Road, Clifton, Bristol BS8 1NU 34 35 36 37 Conflicts of Interest The authors have no conflicts of interest. 38 39 40 Running title: Objective Eye Tracking in the clinic 41

43

44

45

## **Main Text**

- Numerous research studies have demonstrated the scope and value of eye
- 47 movement recording (EMR). There is now potential for EMR to be helpful in a
- 48 range of clinical contexts and it could be developed as a routine part of the
- repertoire of clinical investigations offered by the NHS, at least in tertiary centres.
- We highlight potential uses and challenges below, as a prelude to further
- 51 development and debate.
- 52 Diagnosis
- 53 EMR in patients with nystagmus is already increasingly used clinically and provides
- the only method for identifying the exact waveform[1, 2]. A classic example is
- 55 identifying the characteristic accelerating waveform of infantile nystagmus
- syndrome (INS), which obviates the need for urgent investigations of newly-
- 57 diagnosed nystagmus, saving the patients and the NHS time and money. EMR
- 58 may also indicate the cause of an abnormal head posture (AHP) and identify the
- best option for treatment. For example, an AHP may be adopted to use a null point
- in subclinical, previously undiagnosed INS, or to put an eye into adduction if the
- 61 patient has latent nystagmus.
- However, EMR can help in the management of patients other than those with
- 63 nystagmus. Examples include:

- In Parkinson's disease, EMRs of saccades help differentiate between dementia
- with Lewy bodies, progressive supranuclear palsy, corticobasal degeneration, and
- 66 multiple system atrophy[3].
- 67 EMR will differentiate between Gaucher Disease Type 1 and Type 3[4]. This is
- particularly important, as there are different treatment pathways for these patient
- 69 groups. Abnormal EMR metrics have also been reported in children with three rare
- 70 metabolic diseases: Tyrosinemia III, Niemann Pick C and Morquio syndrome[5, 6] –
- 71 potentially allowing treatment to be started earlier in the disease process[6].
- 72 In psychiatry, EMR performance on the antisaccade task is affected (see:[7]) and
- 73 EMR metrics have been used to classify cases of schizophrenia vs controls with
- 74 87-98% accuracy [8] which again may allow earlier and more accurate diagnosis,
- with earlier treatment and support.
- 76 Screening of at-risk individuals
- 77 There is a growing body of evidence that EMR may be useful in the screening of
- 78 individuals at risk of disorders including Huntington's[9], Alzheimer's[10, 11] and
- 79 Parkinson's[12] Diseases.
- 80 Monitoring of disease progression and of response to treatment
- 81 The EMR abnormalities in Niemann Pick C, including curved saccades, increase in
- magnitude with disease severity suggesting that these measures would also be
- useful in monitoring disease progression. Also, in Parkinson's Disease, the extent
- of EMR abnormalities is related to disease progression[13] and responsiveness to
- 85 treatment[14].

Although these results are encouraging, it is likely that EMR alone will only rarely, if ever, be used as the only diagnostic criterion. However diagnostic pathways which include EMR alongside, for example MR imaging[15], are likely to be shorter and more accurate. Whilst the individual conditions may be rare, such as the metabolic disorders, there are a much larger number of patients who present with early or non-specific difficulties in whom treatable metabolic or neurological disease needs to be ruled out, and therefore, specialist services that care for many patient groups may benefit from access to reliable EMR within the NHS. The objective and quantitative measurement of eye movements has a long history dating back to the early 20th Century[16]. Early methods were uncomfortable and invasive, and analysis of the resulting data was time-consuming. However, the advent of both powerful personal computing and fast video-based recording systems has led to a step-change in the last 15 years in this technology. EMR has become standard in a wide range of settings including Consumer Research, Human-Computer Interaction and Virtual Reality. Alongside this, work on both the neurophysiology of eye movement control[17] and the detailed study of human eye movement behaviour[18] means that we can map this visual-motor behaviour onto the patterns of activity across a well studied and extensive brain network. Routine recording of eye movements in a specialist clinical setting is now therefore technically feasible and would provide a sensitive, quantitative and objective method to aid diagnosis and management for a range of patients. However, despite this potential benefit as a clinical tool, there are considerable challenges associated with both introducing eye tracking into clinical practice and making it cost-effective. We are still some way from having eye tracking hardware that is able to successfully record the eye movements of every patient, whatever their age and

86

87

88

89

90

91

92

93

94

95

96

97

98

99

100

101

102

103

104

105

106

107

108

109

level of ability. We need a common suite of behavioural assays that are agreed upon by the wider community, with normative data[19].

We would need to identify which groups of staff would carry out the assessments, what training they would need, and how and by whom the resulting data should be reported. One model is to develop inbuilt test paradigms and proforma reports that include normative data, to limit the expertise required by the individual setting up the test and make EMR accessible to a range of users. However, this highlights the important issue of expertise in interpreting clinical eye movements. EMR may be used to look for very specific abnormalities in an individual patient and a targeted approach (as opposed to a general battery of tests) may be important for efficiency and to address the key clinical question for that patient, especially for children. The choice between a targeted or comprehensive approach requires both technical ability and specific expertise. Training is required, but experience is also important (as any clinician knows). Currently, there is no training offered and no recognised training pathway. One possible route is to set up training for eye movement clinical scientists, which could eventually become registrable with the Health and Care Professions Council (HCPC). As an example, one of us (CH) is registered with the HCPC as a 'Clinical Scientist' (which is a protected title) with designated expertise in eye movements (the only one we are aware of). This avenue could be explored as a way forward to formalise (and regulate) clinical oculomotor expertise. EMR is already widely used in advertising, the aviation industry, rehabilitation

services, computer gaming and virtual reality equipment. The time has come to

explore how best to deploy this technology to the benefit of patients and the NHS.

134

111

112

113

114

115

116

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

## 136 **References**

- 138 1. Papageorgiou, E., McLean, R. J., Gottlob, I., *Nystagmus in childhood.* Pediatric
- 139 Neonatology, 2014. **55**: p. 341-351.
- 140 2. Dunn, M., Clinical assessment of nystagmus. Optometry Today, 2016. **56**: p. 80-85.
- 141 3. Armstrong, R. A., Oculo-visual dysfunction in Parkinson's disease. Journal of
- 142 Parkinson's disease, 2015. **5**(4): p. 715-726.
- 143 4. Harris, C. M., Taylor, D. S., Vellodi, A., Ocular motor abnormalities in Gaucher
- 144 *disease.* Neuropediatrics, 1999. **30**: p. 289-293.
- 145 5. Blundell, J., Frisson, S., Chakrapani, A., Kearney, S., Vijay, S., MacDonald, A., ... &
- Olson, A., Markers of cognitive function in individuals with metabolic disease:
- 147 Morquio syndrome and tyrosinemia type III. Cognitive neuropsychology, 2018. **35**(3-
- 148 4): p. 120-147.
- 149 6. Blundell, J., Frisson, S., Chakrapani, A., Gissen, P., Hendriksz, C., Vijay, S., Olson,
- 150 A., Oculomotor abnormalities in children with Niemann-Pick type C. Molecular
- 151 Genetics and Metabolism, 2018. **123**: p. 159-168.
- 152 7. Hutton, S. B., Ettinger, U., The antisaccade task as a research tool in
- psychopathology: a critical review. Psychophysiology, 2006. **43**: p. 302–313.
- 8. Benson, P.J., Beedie, S. A., Shephard, E., Giegling, I., Rujescu, D., St Clair, D.,
- 155 Simple Viewing Tests Can Detect Eye Movement Abnormalities That Distinguish
- 156 Schizophrenia Cases from Controls with Exceptional Accuracy. Biological Psychiatry,
- 157 2012. **72**: p. 716-724.
- 158 9. Blekher, T. M., Yee, R. D., Kirkwood, S. C., Hake, A. M., Stout, J. C., Weaver, M. R.,
- 8 Foroud, T. M., Oculomotor control in asymptomatic and recently diagnosed
- individuals with the genetic marker for Huntington's disease. Vision research, 2004.
- **44**(23): p. 2729-2736.

- 162 10. Crawford, T. J., Higham, S., Renvoize, T., Patel, J., Dale, M., Suriya, A., Tetley, S.,
- 163 Inhibitory control of saccadic eye movements and cognitive impairment in
- Alzheimer's disease. Biological Psychiatry, 2005. **57**(9): p. 1052-1060.
- 165 11. Boxer, A. L., Garbutt, S., Seeley, W. W., Jafari, A., Heuer, H. W., Mirsky, J.,
- Hellmuth, J., Trojanowski, J. Q., Huang, E., DeArmond, S., Neuhaus, J., Saccade
- abnormalities in autopsy-confirmed frontotemporal lobar degeneration and Alzheimer
- disease. Archives of Neurology, 2012. **69**(4): p. 509-517.
- 169 12. White, O. B., Saint-Cyr, J. A., Tomlinson, R. D., Sharpe J. A., *Ocular motor deficits in*
- 170 Parkinson's disease. II. Control of the saccadic and smooth pursuit systems. Brain,
- 171 1983. **106**(3): p. 571-587.
- 172 13. Jankovic, J., Parkinson's disease: clinical features and diagnosis. Journal of
- neurology, neurosurgery & psychiatry, 2008. **79**(4): p. 368-376.
- 174 14. Hood, A. J., Amador, S. C., Cain, A. E., Briand, K. A., Al-Refai, A. H., Schiess, M. C.,
- 175 Sereno, A. B., Levodopa slows prosaccades and improves antisaccades: an eye
- 176 movement study in Parkinson's disease. Journal of neurology, neurosurgery &
- 177 psychiatry, 2007. **78**(6): p. 565-570.
- 178 15. Rodrigue, A. L., Schaeffer, D. J., Pierce, J. E., Clementz, B. A., McDowell, J. E.,
- 179 Evaluating the Specificity of Cognitive Control Deficits in Schizophrenia Using
- 180 Antisaccades, Functional Magnetic Resonance Imaging, and Healthy Individuals
- With Poor Cognitive Control. Frontiers in Psychiatry, 2018. 9: p. 107.
- 182 16. Wade, N. J., Tatler, B. W., Origins and applications of eye movement research., in
- The Oxford Handbook of Eye Movements, I. D. Gilchrist & S. Everling, Eds. 2011,
- 184 Oxford University Press: Oxford.
- 185 17. Wurtz, R. H., Using perturbations to identify the brain circuits underlying active vision.
- Philosophical Transactions of the Royal Society B, 2015. **370**: p. 20140205.
- 187 18. Liversedge, S.P., Gilchrist, I. D. & Everling, S., The Oxford Handbook of Eye
- 188 *Movements*. 2011, Oxford: Oxford University Press.

189	19.	Antoniades, C., Ettinger, U., Gaymard, B., Gilchrist, I. D., Kristjansson, A., Kennard,
190		C., Leigh, J., Noorani, I., Pouget, P., Smyrnis, N., Tarnowski, A., Zee, D. &
191		Carpenter, R. H. S., An internationally standardised antisaccade protocol for clinical
192		<i>use.</i> Vision Research, 2013. <b>84</b> : p. 1-5.
193		
194		
195		
196	Footr	notes:
197	None	
198	Contributors:	
199	All authors contributed to the drafting and/or revision of this article. The manuscript	
200	was coordinated by RC, IDG and CW.	
201		
202	Funding:	
203	The w	ork was supported by a grant from the UK Engineering and Physical
204	Scien	ces Research Council (EP/M000885/1) to the Bristol Vision Institute which
205	suppo	orted RC and a one day workshop on this topic at the University of Bristol on
206	24 Ap	ril 2018. CW is supported by a NIHR senior research fellowship (SRF208-
207	015).	
208		
209	Comp	peting interests:
210	None	

Ethics approval:
Not applicable
Provenance and peer review:

Not commissioned; externally peer reviewed.