Visual problems in children born to opioid-dependent mothers have been described for decades. The earliest reports were from the USA, and described nystagmus (shaking or wobbling eyes) (Perlstein 1947, Chavez 1979, Rosen 1982, Johnson 1984) and strabismus (squints) (Chavez 1979, Rosen 1982, Johnson 1984, Nelson 1987) in children of heroin-addicted mothers prescribed methadone in pregnancy, many of whom were polydrug misusers. Dominguez et al described nystagmus and squint in two infants exposed to heroin and to heroin and cocaine respectively (Dominguez 1991). Subsequently, similar reports emerged from Europe and Australia as well as the USA, also describing nystagmus (Gaillard 2002, Lloyd 2006, Mulvihill 2007, Hamilton 2010) and strabismus (Gill 2003, Lloyd 2006, Mulvihill 2007, Hamilton 2010) in children exposed in utero to methadone and usually to additional illicit drugs.

By 2008, the only available data on vision following methadone exposure came from retrospective, observational studies. We therefore ran the Vision In Drug-exposed Infants (VIDI) study in Glasgow, Scotland, a constituent nation of the UK. The VIDI study investigated 150 infants at birth and at six months, 100 of whom were born to opioid-dependent mothers prescribed maintenance methadone during pregnancy, and 50 comparison infants. At this time (2008–9), an estimated 16,000 Scottish women of child-bearing age misused opioids and other drugs (Hay 2009, Advisory Council on the Misuse of Drugs 2003) and around 600 children each year were exposed to opioids in utero (Information Services Division 2011). Pregnant, opioid-dependent women in the UK were commonly prescribed maintenance methadone (Department of Health 2007) as part of a harm reduction programme. The only established adverse effect on the child is acute withdrawal (neonatal abstinence/withdrawal syndrome, NAS or NWS) (Department of Health 2007).

In utero drug and alcohol exposure was established by maternal and neonatal toxicology, making the VIDI infants a uniquely well-understood cohort (McGlone 2013a). Significantly impaired visual evoked potentials (VEPs) were noted at birth in opioid-exposed infants (McGlone 2013b), and 40% also had significant clinical visual problems at six months of age vs 9% of comparison infants (McGlone 2014). These findings were notified to the Chief Medical Officer, Scotland and to the consultation panel1 for the review of UK clinical guidelines (Department of Health 2007). Meanwhile, further evidence of visual sequelae in children exposed in utero to methadone and usually to additional illicit drugs continued to emerge (Gupta 2012, Tinelli 2013, Cornish 2013, Yoo 2014, Joy 2015). A Norwegian study found slightly impaired smooth pursuit (eye movements) in children exposed to buprenorphine or methadone and to tobacco (Melinder 2013), and a UK study noted high rates of absent binocular vision (Cornish 2013). Most recently, nystagmus or strabismus was noted in children born to mothers using buprenorphine, either medically or illicitly, during pregnancy (Kivistö 2015). Impaired growth (Mactier 2014), neurodevelopment (McGlone 2015) and neurobehaviour (Baldacchino 2014) have also been described in methadone and poly-drug exposed children.

The oldest of the 150 children enrolled at birth in the VIDI study are now eight years old and during 2017 and 2018 we will re-investigate their vision to understand better the nature of any lasting deficits. We aim to define the natural history of any visual abnormalities, to map the findings to the known prenatal drug exposure and infant visual findings for each child, and to test whether the nature of any visual abnormalities can inform possible models for the causative mechanism.

It is biologically possible that methadone independently contributes to visual problems in exposed children (Farid 2008). In the current cohort of children, neonatal VEP abnormalities were independently associated with maternal prescribed methadone, although only nine children were exposed exclusively to methadone (McGlone 2013b). Two cases of nystagmus have been reported in children exposed only to methadone as established by repeated maternal urine toxicology (Tinelli 2013). However, in almost all studies, including the current study, confounding maternal use of illicit drugs, tobacco and alcohol hamper identification of any causal link (Aylward 1982, Hutchings 1985). Since prescribed methadone leads to better health outcomes for pregnant women and their infants (Minozzi 2013, Jones 2013), any causal link with visual problems should be weighed against the benefits.

Heroin misuse and methadone prescribing peaked in Scotland in 2008 and 2011 respectively and is now falling (Information Services Division 2016). However, worldwide in utero opioid exposure is increasing: this is partly due to wider introduction of harm reduction programmes using maintenance opioids (Harm Reduction International 2016), and partly due to the opioid epidemic—heroin and prescription analgesia—in North America, Europe and Australasia (Lyapustina 2017). One third of women in the USA of reproductive age take prescription opioids (Ailes 2015). As a result, NAS globally has reached epidemic proportions (Kolodny 2015, Allegaert 2016, Pryor 2017). It is plausible that a proportion of these opioid-exposed children will develop visual problems. Impaired vision is detrimental to education and employability (Hatton 1997, Shaw 2007) and adds to co-existing problems of social deprivation in vulnerable children.

Re-examining the VIDI study children will provide unique, new and important data by linking prenatal drug exposure to visual outcome at eight years of age. These data may carry great importance if the current global NAS epidemic leads to more childhood visual impairments. If visual impairment is linked to opioid-dependency in pregnancy, revised advice should be given to women. If methadone is implicated, a rethink of prescribing policy would be indicated.

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