Supplementary data to Authors' reply

The Relative Afferent Pupillary Deficit

The earliest description of the relative afferent pupillary deficit, a bedside test, is credited to the Scottish Ophthalmologist Robert Marcus Gunn (1850-1909) who was jointly appointed at two London Hospitals: Moorfields Eye Hospital and the National Hospital for the Paralysed and Epileptic, Queen Square. The technique he described [1], now known as "pupillary escape", has been largely replaced by the modification known as the "swinging flashlight test" introduced by Levatin [2]. Both authors emphasised that the test is not reliable when both eyes are affected.

The pupil examination should be performed in a dimly lit room with a bright torch (figure). A strong RAPD can readily be detected (figure and video 1).

It is more challenging to detect a weak relative afferent pupillary deficit (video 2). There are at least three methods which help elicit a weak relative afferent pupillary deficit. As referenced, but not further discussed in our position paper, a 0.3 log unit neutral density filter will amplify the relative afferent pupillary deficit response in the affected eye but not when held in front of the fellow, unaffected eye [3] . Alternatively, the clinician can shorten the interval of the swinging light in what is described clinically as "stun the pupil", effectively catching it in mid-constriction to show the dilatation, the hallmark of a relative afferent pupillary deficit. On rapid illumination of the other eye, dilatation of the pupil within the approximate 3-s interval can also indicate a weak relative afferent pupillary deficit (video 2). A pitfall of that approach is the physiological oscillation of the pupil (hippus) which can be mistaken as a relative afferent pupillary deficit (video 3). To double check for consistency of the examination it is also helpful to check if there is a reverse relative afferent pupillary deficit. The reverse relative afferent pupillary deficit shows constriction of the better eye when the swinging light is brought back from the affected eye to the better eye. However the absence of relative afferent pupillary deficit does not mean there is no afferent deficit. With symmetric pathology in both eyes, there will be no relative afferent pupillary deficit[3; 4] . In this situation a practical complementary bedside test is the light-near dissociation [5]. All light-near dissociations are due to some failure of the light reaction, which spares the near reaction (accommodation). Assuming no efferent pupillary dysfunction exists, a positive bilateral light-near dissociation in a patient with vision loss due to presumed bilateral optic neuritis without a relative afferent pupillary deficit should be considered as an indirect sign of a bilateral symmetric afferent deficit. It is challenging, but possible, to demonstrate a relative afferent pupillary deficit in anisocoria and other pupil pathologies (e.g. Holmes-Adie's pupil, an eye with third nerve palsy or a post-surgical pupil, a Horner syndrome) if all steps above are followed.

Of note, seeing a relative afferent pupillary deficit in a person with a darkly pigmented iris can be challenging. In this situation an additional light source can be shone tangentially to the anterior chamber, thus illuminating the iris with minimal illumination of the retina. If available, binocular infrared pupillometry is helpful [6] [7]. The infrared camera available with an optical coherence tomography (OCT) device also permits for binocular assessment of the pupil response, the video recording of which can average out pupillary oscillations (hippus) [8]. By contrast, most modern handheld commercial pupillometry devices are unilateral, do not permit control for accommodation, or both, which is a limitation [9] [10]. Other options include 3D pupillometry OCT [11] and a haploscope-based binocular set-up [12]. With rapid development of camera technology in handheld devices and smartphones [13] , and access to machine learning supported pattern recognition [14], we anticipate that the clinical assessment of relative afferent pupillary deficit will become more accessible and standardised.

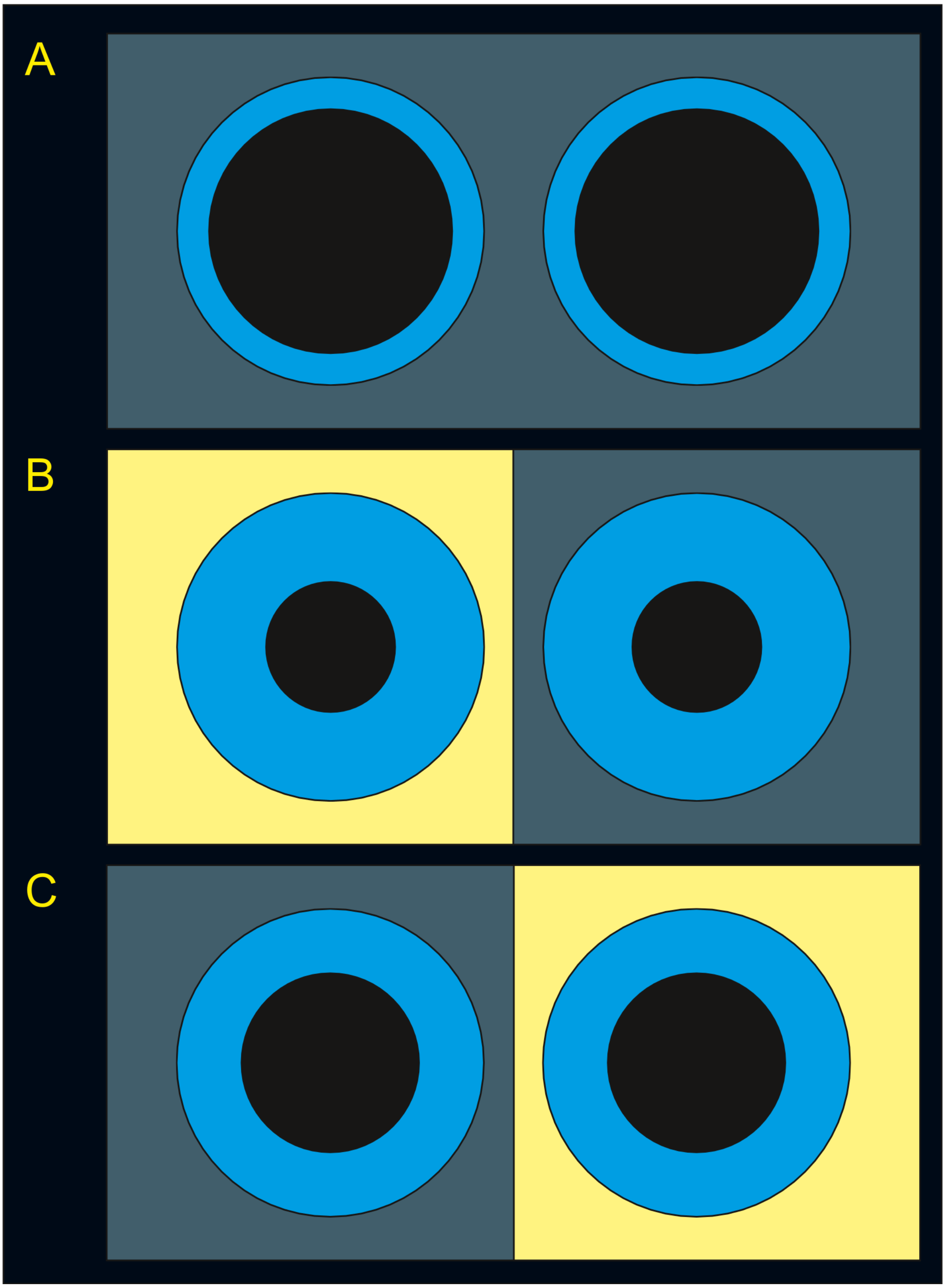

Figure: Relative Afferent Pupillary Deficit

(A) First, to avoid mistaking an anisocoria (physiological or pathological) for a relative afferent pupillary deficit, both pupil sizes are measured in dark. Accommodation should be normal. To avoid misinterpretation of the pupil sizes the person who is being examined is asked to look in the distance. Otherwise normal accommodation of the pupils will compromise assessment of the relative afferent pupillary deficit (see video 1). Next, illuminate each pupil with a bright light source separately, carefully preventing stray light from one eye to the other. This is called the swinging flashlight test because the light is moved (swung) alternating between both eyes (B,C). The pause in between removing the light source from one eye and illuminating the other eye is relevant, but differs in between individuals. A strong relative afferent pupillary deficit will readily be seen if one gives the pupil enough time to start dilating, which occurs within about 3 s in most individuals. Therefore, illuminating the other eye after about a 3-s gap will cause pupil constriction. If the first pupil movement is, however, dilation, then this is a relative afferent pupillary deficit. In the figure, a strong left relative afferent pupillary deficit is illustrated (C).

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