2016 International Orthoptic Congress Burian Lecture: folklore or evidence?

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Burian Lecture:
Folklore or Evidence?

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ABSTRACT

The theme of the 2016 Burian Lecture is how our understanding of strabismus has been changed by the research carried out in our laboratory in Reading over the years. Accommodation and convergence are fundamental to Orthoptics, but actual responses have often been very different to what we had expected. This paper outlines how our laboratory's understanding of common issues such as normal development of accommodation and convergence, their linkage, intermittent strabismus, anisometropia, orthoptic exercises and risk factors for strabismus have changed. A new model of thinking about convergence and accommodation may help us to better understand and predict responses in our patients.

KEY WORDS

Accommodation Convergence AC/A CA/C Binocular Vision

Hermann Burian died just before he saw the final published version of the seminal textbook he wrote with Gunter von Noorden in 1974 (Burian & von Noorden 1974). It was a major influence on me and my colleagues as I qualified and studied for my Orthoptics teaching qualifications. Prior to its publication, the literature on the science behind clinical aspects of binocular vision was sparse and often written by leading ophthalmologists based on their own long experience. "Binocular Vision and Ocular Motility" came out at a time when Orthoptics was moving into a scientific world where *evidence* was primary. When I qualified as an Orthoptics teacher, I had read nearly everything ever written on strabismus. Thankfully, that would now be impossible.

Orthoptics, however, still adheres to many handed-down traditions and "folklore", which have persisted because nobody has questioned them. Orthoptists pride themselves on their clinical skills and expertise in a specialist area found challenging by other professions, but sometimes we have not appreciated that because Orthoptics is "our" specialism, orthoptists must drive the baseline research. My lecture will concentrate on how many fundamentals I "knew" have proved to be very different to how I was taught. I now think about many aspects of Orthoptics in completely differently from the way I used to. I hope this lecture inspires others to challenge more things currently taken for granted.

The following sections outline how the research from our lab has led us along a journey away from some long-held assumptions. Each section addresses an apparently obvious fact I had assumed was true and which our work has subsequently questioned or significantly modified.

"Any esotropia in a baby is probably abnormal".

My daughter had a large intermittent esotropia in her first weeks, which subsequently completely resolved. My doctor and community nurse were unconcerned, but my professional training told me to worry because existing literature suggested that, if anything, exotropia was the norm in neonates (Sondhi et al. 1988). The leading orthoptist at the time, Joyce Mein, suggested I try to find out more, so I have her to thank for my whole subsequent research career. A survey of orthoptists observing their own babies in their first weeks of life revealed that, indeed, many infants' eyes were intermittently misaligned and convergent in early infancy, with no apparent damage to their binocular vision (Horwood 1993). Subsequent research showed that these intermittent misalignments were a normal part of learning to converge, and more importantly, *diverge* to targets moving in depth (Horwood 2003a, Horwood 2003b). Both never showing intermittent misalignments, or being slow to grow out of them, carried slightly increased risk of later abnormality (Horwood & Williams 2001). In normal development intermittent misalignments should have resolved completely by the time the stereopsis described by Birch et al.(1983) emerges at 12-16 weeks.

These early studies eventually led to a PhD supervised by my long-term mentor and co-author Professor Patricia Riddell. Her development of the Infant Vision Laboratory at the University of Reading for research into the development of accommodation (A) and convergence (C) in a typical infants (Riddell et al. 1999, Turner et al. 2002) and gave us the perfect opportunity to look deeper into what was driving neonatal misalignments.

"Neonatal misalignments probably relate to inaccurate use of early accommodative convergence".

Theoretical understandings and the evidence at the time suggested that misalignments would relate to early accommodative vergence: as infants started to accommodate, their response to blur would drive the esodeviations, which weak emerging fusion would fail to fully control. Our photorefraction method allowed us to catch some of these misalignments on camera and measure how much they related to accommodation. If blur and emerging AC/A (accommodative convergence (AC) driven by accommodation to blur) linkages were responsible, they would be more frequent when monocular (without the controlling influence of binocular vision (BV)), and they would be found at the same time as accommodation for near fixation. They were more common when the infants were monocular, but were also more common as they looked off into the distance *after* near fixation and were *rarely linked to accommodation at all* (Horwood & Riddell 2004).

If it was not a response to a disparity stimulus, or an accommodative one, what was left? Could it be motion cues or other "proximal" cues?

The Infant Vision Laboratory Remote Haploscopic Autorefractor

Further funding enabled us to build an experimental setup to tease out the relative weighting of the three main cues to convergence and accommodation, and which was naturalistic enough to be used across the whole lifespan, from premature infants to presbyopes. This apparatus enables us to present blur, disparity and proximal/looming cues in all eight possible combinations. By presenting a target to one or both eyes only we can remove or allow disparity cues; by using a blurry Gabor patch or a detailed target we can minimise or present blur cues; and by allowing the target to be seen to move and loom, or scaling it for distance and covering it during movement we can manipulate proximal /looming cues.

---Figure 1--

We can therefore look at normal, naturalistic "both eyes open" responses, three cue conditions where one cue is removed but the other two are still present, three further conditions where a single cue is presented in isolation, and a "minimal cue" condition which assesses influences we cannot control, such as change in luminance or "top down" influences. In this way we can assess the effect of any cue in two ways (when removed, or when presented as the only cue). We use a PlusoptiX SO4 photorefractor in PowerRef II mode to capture objective, continuous and simultaneous vergence (in metre angles (MA))[1] and accommodation in both eyes (in dioptres (D)). We can also measure objective (response) AC/A and CA/C ratios (the vergence in relation to accommodation driven by blur and the convergence-accommodation (CA) in relation to convergence driven by disparity) tested in otherwise comparable conditions (Horwood & Riddell 2008). Because we started off testing babies and children who cannot be instructed, we have become particularly interested in "what comes naturally" – and are constantly surprised by how different responses are from what the adult literature had led us to expect (Horwood & Riddell 2010).

"Accommodation drives most of the total convergence, so accommodative convergence is important for everyone"

In 1893 Maddox (Maddox 1893) wrote that 2/3 of the total vergence response was accommodative vergence driven by the blur of an approaching target (the AC/A linkage); and that a "normal" clinical AC/A ratio is between 3:1 and 5:1 has remained firmly in the literature ever since e.g. Hoyt & Taylor (2012). Indeed, if blur is the only cue it *can* drive 2/3 of the vergence requirement, so there is plenty of supporting literature e.g. (Rosenfield et al. 1995). But blur, disparity and other cues are generally all available in an approaching target, and each can drive up to 100% of the response *on its own*. Normal responses are rarely excessive, so the influence of cues within a complex stimulus must be relatively weighted. We found that in typical adults and older children adding or taking away disparity has a much greater effect than adding or taking away blur or proximal cues. In normal circumstances *disparity* drives most of the vergence *and* accommodation responses (via the CA/C linkage). The vergence and accommodation driven by response to blur (the AC/A linkage), and the

[1] Metre angles are a very useful way of describing the appropriateness of convergence for a fixation distance. They are the vergence equivalent of a lens dioptre i.e. 3MA at ⅓ metre. Although we are more familiar with prism dioptres, a prism dioptre is a different percentage of the target demand in a baby and an adult. A baby with an IPD of 45mm will need 4.5Δ of convergence at 1m, while a large adult with an IPD of 70mm will need to converge 7Δ, while both will be converging 1MA and both needing to accommodate 1D.

role of proximal/looming cues, are much less important. Thus for most people the CA/C relationship matters much more than the AC/A relationship.

"Adult lab research applies equally to naïve adults and children"

The adult literature is full of data showing how influential the AC/A ratio is, but our findings were very different. Was it our method, or the populations we were studying? Every lab starts off by testing typical controls to establish norms, and most use any staff and students easily available , or (even worse) the experimenters themselves. Our lab controls were psychology students, unlike the optometry students and staff used in most of the literature. We were also testing infants and uninstructable children.

We therefore compared a group of orthoptics and optometry students (who would be likely to work out what the experiment wanted them to do even if they were not told) with psychology students with no vision background. Despite identical (minimal) instructions and no prior experience of the lab, the "experts" produced very different and "better" responses, and the difference between the groups increased the more unnatural the situation or stimulus became (Horwood & Riddell 2010). This means that much of the adult literature should be applied to infant and developmental studies with great caution, unless adult controls are as naïve to the experimental situation as the infants and patients.

Developmental Studies

Our lab was set up to study the development of relative cue weighting. Because visual acuity, BV and stereopsis, IPD and refractive error are all changing between birth and adulthood, we were testing predictions that cue weightings might change over time as different cues became available or more accurate at different times. By using the same method for all our participants, we now have a unique and complete dataset from pre-term responses to presbyopia (Horwood & Riddell 2013).

Typical infants have vergence and accommodation responses not significantly different from those of adults by 8-9 weeks of age when viewing our most naturalistic target. But when relative cue weighting was considered over time our predictions of cue use made after the neonatal misalignment studies were largely proved correct. In very early infancy before 10-12 weeks, proximal / looming cues predominate. At this time, acuity is poor, refractive error common and cortical binocularity and stereopsis have not emerged, so looming is probably the most reliable visual cue. In “middle infancy” up to about 12 months of age, all three cues carry broadly similar weighting. This again may be advantageous, to cope with the rapid growth and development of many physical and neurological systems, all going on concurrently but with different timescales. Beyond 12 months disparity takes over as the main cue to drive both vergence *and accommodation* for the remainder of life. Why would it not? The vergence and disparity detection systems are much more precise, with accuracy down to seconds of arc (depth detection measured in millimetres). In contrast, depth of focus means that change in blur is usually is only detectable when it exceeds +/- 0.5D (differences in fixation distance measured in many centimetres for most targets) even in emmetropic individuals.

We have also carried out a study of premature infants, to try to establish whether vergence and accommodation development is hard-wired or learned. If it is hard wired, premature infants will develop normal responses at the same gestational age as if they had been born at term. If it is learned, however, they will develop them at same time after birth (chronological age). We found that the best match between premature and full-term infants was when compared by gestational age, suggesting that vergence and accommodation are hard-wired (Horwood et al. 2015).

If all aspects of visual development occur in parallel this might not matter as all systems mature concurrently. A paper by Jando et al(2012), however, found that at least one aspect of cortical binocularity develops in relation to chronological, not gestational, age. This means that some premature babies may be developing cortical binocularity (and therefore the potential for suppression and all its consequences) at a time when their vergence and accommodation are still unstable, when usually these two motor systems are mature and stable well before stereopsis emerges. Could this be the reason why premature infants have a higher incidence of strabismus?

"Normal people all respond in the same way"

The literature implies that normal responses are stable and repeatable. But careful reading often reveals that many studies are highly controlled, with difficult tasks that could only be carried out after training or practice and careful, or unknowingly biased, selection of participants (who are often "vision people", with a good idea of the experiment aims, practiced in manipulating their vision and trying to be helpful). The task may have been impossible for some. Outlying or unpredicted responses may have been excluded as artefacts or unreliable. Even if none of these reasons for spurious stability apply, error bars are often large, so mean results mask wide ranges of responses.

We test infants, children and naïve adults and their responses are much more variable than we initially expected. At first we were worried that our measurements were inaccurate, but after careful checking, we now are much happier with the idea that "variable is normal". People in the real world without any symptoms or visual problems seem very content with "inaccurate" responses, especially significant blur. They often *can* accommodate normally, but some rarely *do*. We are increasingly interested in when "normal" starts to be "abnormal"?

Our research had led us to increasingly focus on *differences* between people and what turns some people into patients, when others with exactly the same responses are untroubled. A survey of typical young adults using the Convergence Insufficiency (CI) Symptom Survey

(CISS), widely used to assess symptoms in CI (Rouse, Borsting et al. 2004), found almost no correlation between symptoms often associated with CI and actual defects (Horwood et al. 2014). There is no doubt that people with CI get symptoms caused by poor convergence (and which can be monitored using the CISS), but many people also have what most professionals would call CI but without symptoms, while others have identical symptoms without CI.

Could we use this variability to explain the aetiology of strabismus & heterophoria?

Our developmental and typical adult studies showed us that although most people's responses are "disparity driven", some people do respond better to blur or proximal cues. Some respond well to any or all of the single cues, while others only respond well if all cues are available. Could this be a reason why some children squint while others do not, and why patients respond differently to treatment e.g. how an angle changes in response to glasses?

So far, this is proving to be the case. We have shown that vergence and accommodation of specific clinical groups respond characteristically to the different cues, and that responding better to blur or disparity is associated with different diagnoses even if two groups have identical AC/A or CA/C ratios (Horwood & Riddell 2014). Hypermetropia only seems to cause an esotropia if you are a "blur person" and the visual system sacrifices binocular vision in order to keep things clear, while a "disparity person" might sacrifice clearing their vision in favour of keeping straight. Orthoptists treating many accommodative deviations seem to see more "blur people" (for whom the AC/A ratio *does* matter) than exist in the non-clinical world, so perhaps clinicians have a distorted view of normal. Aside from accommodative strabismus, our model can be supported in many different types of concomitant strabismus and heterophoria.

If variable is normal, what makes "abnormal"? We suggest that there is a large envelope of "normal" and that most people do *not* have the fixed relationships between vergence and accommodation suggested by the literature. Only if limits of this envelope are exceeded do symptoms, heterophoria or strabismus become problematical. Significant refractive error, being too strongly "blur driven", being too fixed in AC/A or CA/C linkages so unable to converge without accommodating or vice versa, or having defective BV, would exacerbate risk of developing orthoptic problems. Good "positive and negative relative vergence /accommodation" are just another way of saying that vergence and accommodation are usually able to vary in relation to each other.

"Young people all - and always - accommodate for near"

We should all be familiar with the idea that a certain amount of accommodative lag is typical. But in our lab we are frequently surprised by how variable and extreme this is. While convergence is usually very accurate to approaching targets, accommodation may or may not be equally precise. We have evidence that many children only accommodate when they need to, despite identical vergence responses to targets containing different levels of detail. So if they maintain straight eyes at all times, what does that say about the "fixed" AC/A linkages we are taught?

"Accommodation and convergence have a strongly linear relationship"

While this is generally the case, we sometimes see adults, and often see infants, where accommodation and convergence seem to be acting almost independently. This seems particularly the case for patients with accommodative spasm or medically unexplained loss of vision.

"Modest under-correction of hypermetropia in children is acceptable because they will accommodate to make up the difference"

We studied accommodation in typical children, and a group of hypermetropes both with and without their glasses. Even with fully corrected glasses, many hypermetropes underaccommodated more than non-hypermetropic children for near, and without glasses none "made up the difference". Uncorrected or under-corrected hypermetropes may do more accommodation for near than distance, but most systematically under-accommodate by the amount they are under-corrected (Horwood & Riddell 2011). This is particularly the case for those with accommodative esotropias, who systematically under-accommodate to maintain control. This suggests that under-correction may be less advisable than we thought. It remains to be seen whether a modest amount of under-accommodation *matters* to non-visual aspects of children's lives such as literacy and attention.

"Some distance exotropias "control by accommodation""

It has generally been assumed that some children with intermittent exotropia recruit accommodation to bring about accommodative convergence and so aid control. The clinical evidence for this is that by changing blur, the angle changes; thus minus lens therapy can help control. This would imply that these patients are likely to be more "blur driven". We tested children with distance exotropias (clinically those whose angles increased or control decreased for distance fixation, and whose divergent angle increased with plus lenses for near) when they were controlling their deviations. Most accommodated more than non-strabismic controls to most cues, but when we analysed responses to the separate cues we found that they were accommodating to pure blur cues no differently than the controls (Horwood & Riddell 2012) and were still "disparity driven". What they seemed to be doing was *converging* to control (Firth 2008, Firth et al. 2013, Brodsky et al. 2015) what was, after all, the primary problem; the exotropia. Extra convergence effort leading to additional vergence-accommodation is the more likely explanation for the additional accommodation for these children, especially those with a strong link between vergence and accommodation. Minus lens therapy could well work by correcting any over-accommodation brought about by the effort to converge to control a large deviation, rather than by inducing blur-driven accommodative vergence (Brodsky et al. 2015). Lenses *allow* them to control, rather than *making* them accommodate.

What is more worrying for clinicians is that when the control of intermittent exotropia breaks down for near and convergence to control fails, not only is BV lost, but accommodation also fails (Horwood & Riddell 2012). We suggest that clinicians should ask children more carefully how they know their exotropia has broken down. Many comment on blur, not diplopia. Blur for close work, as well as loss of BV, is another reason why surgery is indicated once decompensation occurs for near.

As a further point, this same mechanism may also account for the occasional convergence excess consecutive esotropias encountered immediately after intermittent exotropia surgery. Sudden reduction of the convergence demand to control a large exodeviation might lead to hypo-accommodation. Now-inappropriate convergence may be the only way to drive adequate accommodation in the post-operative period, so perhaps a near reading addition may be a more logical therapeutic approach than prisms.

"Clinical AC/A Ratios always tell us about Accommodative Vergence"

We routinely collect data about the vergence driven by blur and the accommodation driven by disparity (the AC/A and CA/C relationships and ratios). These are *response* ratios, where the divisor in the formula is the actual response produced, not the stimulus given. Most clinical AC/A ratios are, however, *stimulus* ratios, where we introduce a lens or change of fixation distance and assume the appropriate amount of accommodation has occurred. As outlined above, this is rarely the case and so response ratios are usually much higher. For example,15Δ change in vergence and an assumed 3D of accommodation over the -3.0D lenses of a stimulus gradient ratio leads to a ratio of 5:1; but if only 1D of accommodation has actually occurred, the response ratio is 15:1. A "low" stimulus ratio may be truly low, because accommodation does not influence vergence much, or may be "low" because accommodation has not occurred, so neither has much accommodative vergence.

CA/C ratios are usually ignored by clinicians, because they are almost impossible to measure clinically; but that does not mean they are not important.

When we compared the response CA/C and AC/A ratios which we measure experimentally, and correlated them to near (plus lenses) and distance (minus lenses) clinical gradient AC/A ratios in intermittent exotropia, it was remarkable how poorly they all correlated. The two clinical ratios correlated with each other very weakly, but neither correlated at all with the accurate "true" response AC/A ratio. Surprisingly, the near clinical stimulus AC/A ratio (plus lenses for near) correlated best with the response CA/C ratio (Horwood & Riddell 2013).

We suggest the near AC/A clinical ratio might be a useful clinical way to get an idea of the CA/C ratio which is currently clinically untestable. The mechanism may be thus. We know that the dissociation of the cover test stops convergence and so is most likely to also prevent the accommodation it drives. But the orthoptist stresses keeping the target clear during testing. The only way many children know how to accommodate is by converging too, so they cannot let their convergence relax fully if they are to accommodate, and the full exodeviation fails to appear. The plus lenses introduced in the second part of the test allow clear vision for near without needing accommodation, so convergence can finally relax fully and the angle increases. Therefore the apparent "high AC/A" in intermittent exotropia actually reflects how much convergence is needed to drive accommodation (CA/C).

"Orthoptists know how orthoptic exercises work"

While we all know that eye exercises have a role in convergence insufficiency and heterophoria and most of us have been taught that "relative" methods (convergence in excess of accommodation and vice versa) were the best way of achieving change. There is a huge amount of myth around whether, how, and when eye exercises work, leading to many inter-professional differences in approach – but very little evidence that is not subject to placebo, practice or therapist effects. As a large baseline study, we carried out a study of normal young adults given different eye exercise regimes (including a control, placebo and "just try harder" condition, as well as 5 sets of genuine exercises targeting accommodation, convergence, both together and two "relative" regimes (accommodation in excess of convergence and convergence in excess of accommodation). We then looked at objective changes in accommodation and vergence after two weeks of exercises.

The most effective exercise to improve both convergence *and* accommodation responses were simple convergence exercises concentrating on resolving disparity alone, independent of blur. Blur exercises, those exercising vergence and accommodation in parallel and both "relative" methods, were much less effective. The most effective method of all was just being encouraged to work harder by an enthusiastic tester. So it is clear that more work is needed to see what methods we should be using if we give eye exercises, because the therapist instructions and encouragement may be as important as the exercise (Fray 2013).

"Accommodation is symmetrical"

We even have evidence to show that accommodation is not necessarily consensual. A few years ago by chance we tested a child who had volunteered as a normal control. She proved to have anisometropic amblyopia (Horwood & Riddell 2010), and would have been excluded from recruitment if we had known, but on that day we collected accommodation data before testing her vision. She demonstrated extraordinary accommodation in the amblyopic eye only, which accommodated more in the *distance*, while the other eye behaved normally. This led on to research presented at the 2012 International Strabismological Association meeting in Kyoto to see if this was more than a one-off finding. Briefly, the study found that most anisometropic amblyopes aniso-accommodate to some extent, and around 25% “anti-accommodate” in the amblyopic eye. The more severe the amblyopia and anisometropia, the more common this was, and it also predicted a poorer outcome to amblyopia treatment. The concept that accommodation is always a consensual response is so ingrained in current thinking that few people have considered it as a topic for research, so there is much more to do in this area.

In Conclusion

Over the years, many things I thought were obvious, true or simple have proved to be anything but that. We are fortunate to work in a field of science where there is still great deal we do not know, and I have been fortunate in being given the opportunities to do research, with people who have encouraged me to question.

We should not ignore the mass of literature presenting conventional or traditional views of the BV system built up over many years. Many alternative models and older theory still apply in most, or many, cases and can be replicated in tightly controlled situations. Nevertheless I am constantly surprised how much more flexible the BV system is if it is *not* tightly controlled.

So the conclusions of this lecture are:-

- Don’t believe something because someone tells you it is “well known”.
- Don’t assume the people who taught you are always right.
- Keep asking “why?”, “how?”, “how much?”, “does it really?” and “does it always?”.
- Orthoptists probably have more insight into the characteristics of binocular vision and its abnormalities, so we are the ones able to ask the right questions in the topics that concern us.

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FIGURE LEGEND

Figure 1 The remote haploscopic videorefractor. (A) Motorized beam. (B) Target monitor. (C) Upper concave mirror. (D) Lower concave mirror. (E) Infra-red 'hot' mirror. (F) Image of participant's (P) eye where occlusion takes place to eliminate disparity cues. (G) Plusoptix SO4 PowerRef II. (H) Headrest. (J) Raisable black cloth screen to allow looming cues to be excluded when necessary. Clown and difference of Gaussian targets (to manipulate blur cues) illustrated lower right.

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