The Developing Visual Brain: typical and atypical development

Janette Atkinson

Oliver Braddick

Review paper on development of attention and attention deficits:


Approximately half of your brain is used in everyday visual tasks

We study vision and visual cognition in babies and children because:

• vision develops rapidly in early life and serves as a base for development of cognition, communication, social interactions
• visual measures are often a guide as to how well the whole brain is functioning
• from early measures we can predict how well the brain will function in the future - neurological/cognitive outcome.

Webinar by Jan Atkinson
talk and short video of VDU research
http://www.ucl.ac.uk/neuropsych/InternationalSymposia (under ‘FREE LECTURES’)


The starting point of our research and assessment …

our first child - Fleur Braddick (3 months) in stripy cot


Current and future research…

- ERP measures of typical and atypical brain development, linked to preterm birth
- (EEG linked to fMRI)
- John Wattam-bell et al

New methods, using the Tobii eye tracker for assessing visual sensitivity in children with inherited retinal dystrophy (in future gene therapy trials)
- Marko Nardini et al

Converging approaches?

Behavioural and electrophysiological measures each have limitations and advantages in revealing infants’ visual capabilities

More secure knowledge comes when data from the two methods converge

Behavioural discrimination – preferential looking / habituation

Visual event-related potentials/ visual evoked Potentials (VERP/ VEP)
Research and assessment in the Visual Development Unit

- adult psychophysics & VEP/VERP
- behavioural & VEP tests of normal development
- Infant-structural MRI
- neuro-developmental disorders of childhood
- adult fMRI

[video = The Developing Visual Brain ]

we have put forward neurobiological models of eye-brain visual development

- what are the changes in the brain which are activated when we observe changes in visual behaviour during development?
- what is the plasticity (adaptability) of different brain systems (so that if one brain area is abnormal or damaged can another area take over this function)?
- does the ‘plasticity’ depend on the time of damage? (sensitive/critical periods early in life?)

NEUROBIOLOGICAL MODEL OF DEVELOPMENT

- what changes in the brain underpin changes in behaviour?
- what is the plasticity (adaptability) of different brain systems?

Atkinson & Braddick
- 1984 (Human Neurobiology, 3: 61-74)
- 1994 (Eye 6: 129-135)
- 2000 (The Developing Visual Brain)
What can newborns (first 6 weeks of life) do?

- Good reflexes (subcortically controlled): rooting, sucking, walking, grasp, Moro (startle) - these disappear early in life in normal development
- Eye movements: saccadic tracking following a toy
- Crude auditory localization (subcortical): turn head and eyes towards a voice
- Smell/taste discrimination (preference for certain sugar concentration)
- Imitation of facial/finger movements
- Face preference/ preference for familiar face
- Visual acuity = 1 cycle per degree (1 cm at 57 cm distance)

NORMAL DEVELOPMENT

Subcortical visual system at birth

Cortex starts to function, with different onset times for different systems, between 1-6 months of age.
Onset of smooth pursuit - 4 months

Modes of face processing: Facial expression

- Meltzoff & Moore (1977) and others
imitation of facial gestures by newborns

Possibly newborns have a bias to attend more to higher contrast (in the upper field of view in faces)

Conspec and conlern

Newborn tracking technique

Goren Sarty & Wu, 1975; Johnson et al, 1991

FIG. 7. Which one is mother? (photograph by Ian Bushnell)

Ian Bushnell et al – 2 day olds looked longer at mother’s face than stranger’s face what cues used? - hairline
"EXTERNALITY EFFECT"

Young infants respond to differences in the outer contour of a form more readily than to differences in the internal details.
Development of acuity
Forced choice preferential looking

• behavioural technique
• based on a natural preference e.g. looking at a pattern rather than a grey screen
• forced choice on the part of the observer (not the baby) - stops cheating!

Acuity & Contrast Sensitivity
Forced choice preferential looking
Automated version / Teller/Keeler cards

Simulated acuity viewing face at 50 cm
1-month old

Normative data on acuity development – preferential looking
Simulated acuity viewing face at 50 cm
3-month old

Simulated acuity viewing face at 50 cm
adult

Limits on developing visual acuity:
Receptor density & efficiency

- short outer segment (OS) = inefficient at detecting light
- fat inner segment (IS) = cones aren’t tightly packed = poor spatial sampling of the image
- Development of long fibre = cones displaced to allow dense packing in foveal pit

Most important: neural development

neurons of primary visual cortex

NEWBORN: 3 MONTHS
NORMAL DEVELOPMENT

Subcortical visual system at birth

Cortex starts to function, with different onset times for different systems, between 1-6 months of age.

cortical neurons – and not precortical (subcortical) - show selective sensitivity to:

- orientation
- direction of motion
- binocular disparity (stereopsis)
Steady state visual evoked potentials (VEP) or visual event related potentials (VERP)

- Orientation-reversal VEP significant in first few weeks (3-8 weeks) of life

- Motion-reversal VEP later around 12 weeks

Test for binocular vision - random dot correlograms
record visual evoked potential (VEP) - brain waves - time locked to the change in pattern from correlated to anti-correlated

Onset of Binocular VEP
Median 3-4 months
Development of the visual cortex in early infancy - LOCAL PROCESSING

Different cortical functions all develop post-natally - they don't have a common age of onset

ATTENTION IN INFANTS - FIXATION SHIFTS

NON-COMPETITION: seen in normal newborn infants

COMPETITION: seen only after 4 months of age.


Deficits on competition

- Williams Syndrome
- term-HIE, very preterm infants

Cerebral Palsy


Hemispherectomised infants (one hemisphere removed to relieve intractable epilepsy) - a source of information on subcortical function

Pre-operative

Post-operative (different child)

Infant with hemispherectomy

**IGNORES** target in the damaged half field under COMPETITION

**FIXATES** target in *either* half field under NON-COMPETITION

...so cortex is necessary only for fixation shift under competition

---

**Two cortical visual systems**

- **‘DORSAL’ stream**
  - ‘where?’ ‘how?’ ACTIONS
  - posterior parietal cortex (PPC) (Dorsal Stream)
  - V1

- **‘VENTRAL’ stream**
  - ‘what?’ ‘who?’ OBJECTS
  - inferior temporal (IT) cortex (Ventral Stream)

---

**Dorsal stream**

- Motion
- Global motion processing
- Processing layout in space – visually guided actions
  - ..... where?
  - ..... how?

**Ventral stream**

- Static orientation
- Global pattern processing
- Recognising objects and faces
  - ..... what?
  - ..... who?
Ventral and dorsal cortical streams

Local and global cortical visual processing
- V1: local processing
- Extra-striate visual areas: global processing
- Different cortical streams for static form & motion

fMRI: coherent - incoherent form motion

intraparietal sulcus  V3A middle occipital V5 lingual/fusiform
(schematic) Braddick et al (Current Biology, 2000)

form & motion coherence activate:
- Extra-striate, not striate cortex
- Independent, non-overlapping networks

Direct comparison of form & motion coherence
- Measures of global motion and form performance tap human extrastriate visual function
- .. to track normal human development of global processing...
- .. and ‘dorsal stream vulnerability’ in developmental disorders (Atkinson et al, 1999; Braddick et al, 2003)
High density steady-state VERP recording

• EGI Geodesic sensor net
• 128 channels
• Detect responses to change from incoherent to coherent (global static form or global motion)

Percent of 5 month old infants showing significant responses

- 5 month olds show global motion responses
- Weaker global form responses – reliable in about half the infants

Compare adult & infant results

• different source distributions – adults, global motion on midline; infants, global motion lateral
• global processing is radically reorganized from infancy to adulthood

‘mild/moderate’ prematures vs controls

• Different distribution in preterm infants (mild/moderate MRI) compared to controls (term-born normal infants)
• global MOTION foci are in more lateral locations for premature infants than for controls (term-born infants)
• Delay in reorganization of network – more ‘immature’ MOTION network?
Compare dorsal and ventral streams –
behavioural coherence thresholds

Form coherence

Motion coherence

- What is the least percentage of coherent elements needed to detect the pattern?

[Images of patterns with varying coherence levels]

COMPUTER GAME – ‘FIND THE BALL IN THE GRASS’

Global coherence thresholds for static form (ventral) versus motion (dorsal)

TEST takes 20 mins approx. suitable for all ages above 4 years (mental)

form & motion coherence thresholds

- school-age groups & adults
  ‘find the ball in the grass’ – laptop computer game

VENTRAL – static ‘ball’ on left or right

DORSAL – rotating ‘ball’ on left or right

DORSAL (motion) matures later than VENTRAL (static) in normal children

form and motion coherence norms

concentric patterns

mean & s.e.m

Williams Syndrome

- 1 in 20,000 to 50,000 births
- abnormal morphology - ‘elfin’ like faces
- deletion on chromosome 7 (30 genes approximately including elastin – cardiovascular defects)
- Severe visuo-spatial deficit
- relatively fluent use of language (but initial delays across all domains)
- ‘hyper-social’ personality but fears and obsessions like autism/ASD
- VDU = over 200 WS individuals


ABCDEFV
A(Atkinson) Battery of Child Development for Examining Functional Vision (birth -5 years)

1. General vision tests for all ages e.g. acuity- Teller Cards/ Cambridge Crowding Cards, exam for strabismus, visual attention at distance
2. Age specific tests e.g. visuo-cognitive - shape matching, block construction copying

Advantage: rapid portable test= 20 mins

WS N=103 under 12 years

CAMBRIDGE CROWDING CARDS
Preschool Acuity Test (mental 4-6 years) test distance =3 metres
- gives child acuity comparable to adult letter chart acuity (e.g. Snellen)

Match central letter

Does not need accurate pointing or naming of letters-Suitable for many children with CP

WS - Good at recognizing faces - but not necessarily normal strategy
Williams Syndrome
WS N=97
vision problems: approx 50% of WS children have
- strabismus
- poor focusing
- hyperopic refractive errors
- acuity deficits (amblyopia).
- BUT vision problems are NOT well correlated with severity of spatial deficit

ABCDEFV – age specific tests
VISUO-SPATIAL, VISUO-COGNITIVE & VISUO-PERCEPTUAL TESTS
- object permanence
- shape matching
- embedded figures
- block copying

ABCDEFV
A(Atkinson) Battery of Child Development for Examining Functional Vision
Age appropriate visuo-cognitive tests - shape matching, copying block construction

Screening Programmes
Children who were significantly hyperopic (long/far-sighted) at 9 mo worse than controls at 14 mo and 3.5 years on ABCDEFV
WS child (11 years verbal IQ) attempting to copy 4-brick enclosure

POST/MAIL BOX TASK (adapted from Milner & Goodale)
- Post the card (dorsal stream)
- Match the angle of the slot (same orientation information, ventral stream)

In WS children angular errors and movement planning show marked impairment of posting (dorsal) compared to matching task (ventral)


WS static form vs motion
- ‘find the ball in the grass’ computer game

<table>
<thead>
<tr>
<th>Form coherence</th>
<th>Motion coherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>VENTRAL: WS near normal</td>
<td>DORSAL: WS deficit</td>
</tr>
</tbody>
</table>


‘DORSAL STREAM VULNERABILITY’ IN WILLIAMS SYNDROME

- Post box task – POSTING letter worse than MATCHING letter orientation to post box aperture
- MOTION coherence thresholds higher than FORM coherence thresholds

DORSAL STREAM VULNERABILITY

DORSAL stream - motion coherence poor
VENTRAL stream - form coherence normal

- young Williams Syndrome children$^{1,2}$
- adult Williams Syndrome$^3$
- autistic children$^4$
- hemiplegic children$^5$
- developmental dyslexics$^6$
- fragile X$^7$
- very preterm$^8$
- congenital cataract$^9$
- rod monochromat$^{10}$

$^1$ J Atkinson et al, NeuroReport 8, 1919-1922 (1997)
$^8$ LS Jakaboski et al, Neuropsychologia, 40, 1777-1786 (2007)
$^{10}$ Burton, Nardini & Wattam-Bell et al, ECVP 2012

But, in addition to these dorsal stream deficits, WS individuals have deficits in:

- all visuo-motor tasks
- spatial location memory
- attention and executive
- Perseverative behaviour and obsessions - similar to Autism and Aspergers Syndrome

Brain imaging:

structural MRI in WS

2 WS infants under 3 years:

- enlarged cerebellum (Chiari I)
- abnormal white matter in parietal lobes (abnormal myelination?)

stair descent in WS

- Families of WS consistently report stair descent and walking on uneven surfaces, as areas of difficulty
- dorsal stream necessary to translate visual information into control of action


SPATIAL LOCATION TASK
remember the location of the hidden toy

- adult WS similar to 4 yr olds, don’t use board landmarks
- child 5-11 yr WS - anomalous, some worse than 3 yr olds


ATTENTION IN WS-
FIXATION SHIFTS

Young WS show deficits on competition,


COUNTER-POINTING TASK- Executive Function

1. central fixation target
2. pointing target

WS – deficits on counterpointing
(and young WS on pointing- parietal and frontal circuits)
ATTENTION DEFICITS and the dorsal stream

Overlapping networks - dorsal streams and attention areas

Ventral stream

DORSAL

ATTENTION (EF)

SPATIAL MEMORY

DORSAL

GRASPING

REACHING

DORSAL

Components of three brain attention networks
Can we assess separate different attention networks before age 6 years?

- Equivalent of TEA-Ch for younger developmental ages?
- We have developed the ECAB = Early Child Attention Battery
- Aim: a comprehensive battery of tests to give an ‘individual attention profile’ for each child
- Suitable for mental ages 3-6 years

**ECAB – Early Child Attention Battery**

Measures designed to tap the following components:

- Selective Attention
- Sustained Attention
- Attention Control (Executive Function)

Suitable for mental ages 3-6 years


**ECAB – selective attention**

<table>
<thead>
<tr>
<th>VISUAL SEARCH</th>
<th>FLANKER TASK</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Find all the red apples” (number of targets found in 1 minute)</td>
<td>“Which way is the fish looking?” (time conflict - congruent)</td>
</tr>
</tbody>
</table>

Spatial direction of attention - posterior parietal, esp R
Target selection - anterior cingulate, thalamus

**ECAB – sustained attention**

<table>
<thead>
<tr>
<th>VISUAL SUSTAINED</th>
<th>AUDIO SUSTAINED</th>
<th>DUAL TASK</th>
</tr>
</thead>
<tbody>
<tr>
<td>“say whenever you see an animal”</td>
<td>“say whenever you hear an animal’s name”</td>
<td>“say whenever you see an animal or hear an animal’s name”</td>
</tr>
<tr>
<td>(number of correct responses, 150 slides for 200 ms each at 2 sec intervals)</td>
<td>(number of correct responses, 150 word at 2 sec intervals)</td>
<td>(number of correct responses - 150 image/word pairs at 2 sec intervals)</td>
</tr>
</tbody>
</table>

“bus” “train” “ball” “cat” “shoe” “star”

R parietal & frontal; thalamus
ECAB – attention control (executive function)

VERBAL OPPOSITES
“when you see a cat, say ‘dog’, and when you see a dog, say ‘cat’.” Score by conflict time – congruent time

inhibition of prepotent (familiar) response – prefrontal lobe

Williams & Down’s syndrome participants in ECAB study

<table>
<thead>
<tr>
<th>group</th>
<th>chronological age (years)</th>
<th>mental age (years)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>range</td>
</tr>
<tr>
<td>WS (n=32)</td>
<td>8.45</td>
<td>5.0-15:11</td>
</tr>
<tr>
<td>DS (n=32)</td>
<td>9.76</td>
<td>5:01–14:07</td>
</tr>
</tbody>
</table>

* MA derived from WPPSI subtests: Information, Block Design, Vocabulary, Picture Completion

CLINICAL GROUPS

1. TERM-BORN WITH BRAIN DAMAGE (HIE/focal infarcts)

2. PRETERM, VERY LOW BIRTH WEIGHT (VLBW) INFANTS under 33 weeks gestational age
PRETERM, VERY LOW BIRTH WEIGHT (VLBW) INFANTS

under 33 weeks gestation age

(including PVL - periventricular leukomalacia - associated with Cerebral Palsy)

White matter damage in very preterm born

- Immature blood supply
- Poor autoregulation of blood flow
- Maternal infection
- Ischemia, anoxia
- Neuron death > Glutamate release
- Pre-oligodendrocytes destroyed
- White matter damage & impaired myelination
- Impaired cortical growth

CEREBRAL PALSY/visuo-motor and/or COGNITIVE IMPAIRMENT

Based on Du Plessis & Volpe, 2002

Imaging at birth/term OR-VEP, fixation shift (3-7 mo)
Griffiths, neurological assessment (2-3 yrs)

ABCDEFV (core vision, perception/cognition) (1-6 yrs)
Block construction (spatial cognition) (2-5 yrs)
Frontal function/attention (2.5-5 yrs)

Core vision tests (6 yrs)
Global form & motion (dorsal & ventral function) (6 yrs)
Attention (6 yrs)
Spatial memory (6 yrs)
IQ, NEPSY, movement ABC (6 yrs)

Hammersmith cohort 1
0-6 years correlation?
Imaging at birth/term
OR-VEP, fixation shift (3-7 mo)
ABCDEFV (core vision, perception/cognition) (1-6 yrs)
Block construction (spatial cognition) (2-5 yrs)
Frontal function/attention (2.5-5 yrs)
Predicts neuro at 2-3 yrs
Griffiths, neurological assessment (2-3 yrs)

Hammersmith cohort 2
6-7 years correlation?
Imaging at 5 yrs, 6 yrs
Core vision tests (6 yrs)
Global form & motion (dorsal & ventral function) (6 yrs)
Attention (6 yrs)
Spatial memory (6 yrs)
IQ, NEPSY, movement ABC (6 yrs)

Oxford cohort: 0-3 mo
Ultrasound (preterm)
OR- & DR-reversal VEP (2-5 mo)

Hammersmith cohort 3: 0-2 years
MRI at term
Hi-density VERP; global form motion; ABCDEFV (2-5 mo)
Bimanual, ABCDEFV (10-18 mo)

VDU / Cambridge / Hammersmith / Oxford preterm studies

Preterm study:
Classification of newborn MRI scans

Normal/mild
N = 8
No neonatal lesions; neonatal IVH resolved mild DEHSI or none at term

Moderate
N = 8
any of: moderate or severe DEHSI; moderate DEHSI with ventricular dilation; ventricular dilatation at term neonatal focal punctate lesions; small parenchymal infarction

Severe
N = 10
any of: ventricular dilation requiring intervention; cystic periventricular leukomalacia (PVL), large parenchymal infarction, or infarction within basal ganglia or thalamus

DEHSI:
Diffuse Excessive High Signal Intensity in white matter (T2-weighted MRI) at term equivalent age

25% of infants showing a positive CORTEX OR-VERP response

0 20 40 60 80 100
Severe Moderate Normal/mild

% of infants showing normal FIXATION SHIFTS responses

0 20 40 60 80 100
Severe Moderate Normal/mild


FRONTAL EXECUTIVE FUNCTION
Ex- Premature – 2-5 years
- Hood tubes 3-5 yrs
- detour box 2-4 yrs
- counter-pointing 4+ yrs

% passing age-appropriate tests

100 80 60 40 20 0
Severe Moderate Normal / Mild

ATTENTION TESTS 2-6 years
FRONTAL LOBE TESTS
INHIBITION OF FAMILIAR RESPONSE OR SWITCHING TO NEW STRATEGY
- Hood tubes (invisible displacement)
- detour box (Russell)
- counter-pointing (Atkinson)
- Stroop (“day-not-night”) (Diamond)

DORSAL STREAM VULNERABILITY
PREMATURE: children born before 33 weeks gestation tested at 6-7 years
Significantly more failures on tests with * above.
CURRENT MODEL

DORSAL STREAM / PARIETAL — visuo-motor & motion deficits
DORSAL STREAM / FRONTAL — deficits in attention, inhibition & executive function

VENTRAL pathways for language & visual recognition not impaired
HIPPOCAMPAL impairment connected to dorsal stream

Atkinson and Braddick. From Action to Cognition Progress in Brain Research, 2007

SUMMARY

• Neurobiological MODELS of visual development including dorsal and ventral streams
• special ‘DESIGNER’ (‘marker’) tests to identify delay/deficit in specific visual eye-brain areas in infants and children with perinatal brain damage (term HIE/preterm birth) and developmental syndromes/disorders
• Correlation of electrophysiological & behavioural measures with structural MRI in clinical groups
• Neurocognitive profile in developmental disorders – dorsal stream vulnerability

• global motion vs form — an indicator of dorsal stream vulnerability
• in preterm-born and Williams Syndrome (and possibly many other disorders) — global motion deficit is accompanied by visuomotor and attention deficits (higher levels of dorsal stream(s))
• …. including deficits of frontal control (executive function)

These tests can be used as ‘early surrogate outcome measures’ in trials assessing:
- recovery from early brain damage
- effectiveness of treatment and remediation programmes
120 INFANTS/ YOUNG CHILDREN WITH ‘EVOLVING’ CEREBRAL PALSY

- Randomized control trial of dietary supplement – long chain polyunsaturated fatty acids to increase neuronal growth
- choline, UMP- uridine-5 monophosphate, DHA- docosahexaenoic acid + supportive vitamins & minerals)
- (UMP+DHA+choline= phospholipid in neuronal membranes)

JA + OB with Peter Sullivan, Morag Andrew, Jeremy Parr, - Oxford Paediatrics, Oxford John Radcliffe Hospital

END

Thank you!

- Colleagues in Visual Development Unit, particularly our co-PI John Wattam-Bell
- Colleagues in Uppsala, Pisa, Rome, Oxford & Hammersmith Hospital
- Support from MRC, ESRC, Williams Syndrome Foundation & Cambridge, UCL & Oxford University
- Families and children for patient co-operation