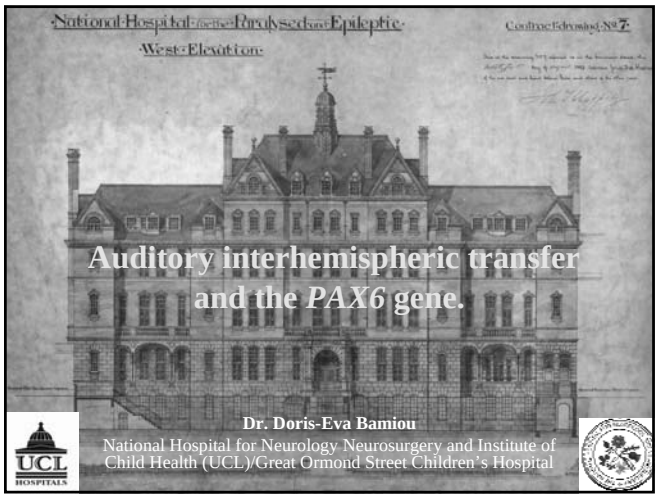
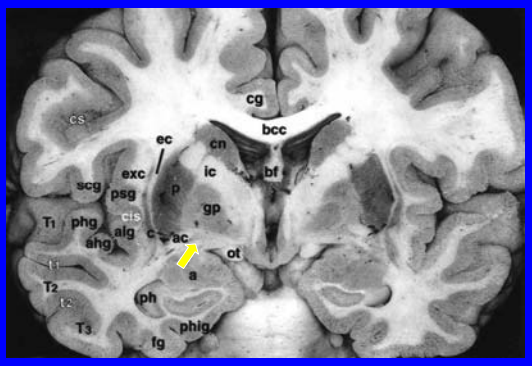



## Lecture outline

- Introduction
  - The interhemispheric pathway in the auditory brain
  - The *PAX6* gene
- *PAX6* case and group studies (adult – children)
- Discussion
- Future studies

## The interhemispheric pathway




## The corpus callosum and the anterior commissure

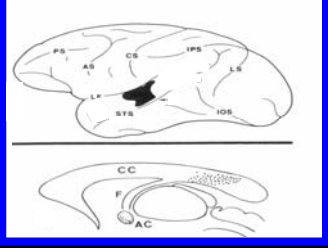
- The corpus callosum is the largest fiber tract in the brain (200,000,000 fibers in humans)
- The human anterior commissure average area is 1% of the CC.
- Both contain heavily myelinated fibers that connect the two hemispheres.
- Vast majority of fibers establish excitatory synapses
- Fibers from cortices with more differentiated lamination patterns travel in the corpus callosum and fibers from less differentiated cortices travel in the anterior commissure.

## Role of the CC and AC

- ?midline fusion (but callosal fibers from sensorimotor cortices few)
- ?co-ordination of subtle processing between the 2 hemispheres
- ? contribution to specialisation of R versus L brain → ↑processing capacity of brain

## Auditory interhemispheric fibres in CC, AC

- Caudal portion of corpus callosum: from primary and secondary auditory cortices
- Anterior commissure: from mid portion of STG - adjacent superior sulcus (Pandya, Seltzer 1986)



## Prenatal development of the CC and AC

- The corpus callosum starts developing between 8 to 17 weeks of gestation age, anterior (genu) to posterior (splenium) growth pattern (Rakic and Yakovlev 1968).
- CC and AC connections will initially develop through a phase of exuberance (? plasticity of the developing brain ) followed by selective elimination

## Post-birth age-related changes of the auditory interhemispheric pathway

- Neuronal differentiation will be complete by the time of birth
- Elimination of fibers will continue (Innocenti 1986; Innocenti 1991 – check; La Mantia and Rakic 1994).
- elimination is signal driven (from thalamic afferents) (Innocenti, 1991).
- ? progressive elimination is reflected by decreasing levels of neural activity evoked by complex cognitive tasks with maturation (PET% studies) (Chugani et al, 1987).

## Post-birth age-related changes of the auditory interhemispheric pathway

- Size corpus will continue increasing until 3rd decade of life (Pujol et al., 1992),
- Relative increase in the number of large (diameter > 1µm) and very large (diameter > 2µm) diameter fibers with increasing age at least until the seventh decade of age in humans (Aboitiz et al., 1996) ? related to the establishment of automatic neural circuits.
- The observed age-related increase for large and very large fibers is seen in the connections between higher order and basic sensory auditory areas respectively in females (Aboitiz et al., 1996).
- Size will gradually decrease after the 4rth decade of age, with posterior areas maintaining a more stable size with aging than anterior areas (Pujol et al., 1992; Paraschos et al., 1993).

## Post-birth age-related changes of the auditory interhemispheric pathway

- Myelination, i.e. encasement of the axons by myelin sheaths, leading to faster neural conduction, will occur in a posterior to anterior pattern
- ?reflecting increasing levels of activity and complexity of interaction between the infant and the environment (Yakovlev and Lecours,1967).
- Completion of myelination will occur later than for other cortical fiber tracts, and may not be complete until 10 years of age or older (Yakovlev and Lecours,1967).

## The interhemipsheric pathway in audition

- The functional role of the corpus callosum and anterior commissure in audition has been examined in patients who have had these pathways sectioned.
- These subjects typically give:
  - normal results in monaural speech tests
  - severely reduced left ear performance in dichotic digits and CVs
  - increased right ear performance in dichotic rhyme tests.

## Dichotic tests in patients with commissurotomy – an explanation

- Language perception takes place in the left hemisphere
- In the monaural situation both the ipsi- and contralateral pathway are functional for sound transmission
- In the dichotic situation, the contralateral pathway becomes dominant in auditory speech signal transmission.

## Kimura's model

## Attentional modulation of dichotic speech test results

- R ear addvantage may increase by focused attention to the right ear. focused attention to the left ear will result in an increased left ear score(Hugdahl and Andersson, 1986).
- A PET study: decreased activation of primary and secondary auditory cortices in the forced vs. the non-forced listening condition ? facilitation of callosal transfer during focused attention (Hugdahl et al, 2000).
- Patients with lesions of the corpus callosum show lack of benefit from focused attention to the left ear on a dichotic CV task, (Pollman et al., 2002).
- Left ear performance in dichotic tests under the left ear forced attention condition may reflect callosal transfer efficiency (Hugdahl 2003) – both sensory and other input

## Pattern test results in in patients with commissurotomy

- The right hemisphere determines the pattern of the sequence of sounds as a gestalt
- The labeling of the sequence happens in the left (language) hemisphere
- Thus, tasks that require labelling of sound sequences depend on transfer of information from the right to the left hemisphere via interhemispheric commissures.

## Congenital aplasia of the interhemispheric pathway

- Subjects with callosal agenesis, with or without an anterior commissure, may suffer from a range of central auditory deficits,
  - deficient phonological processing
  - impaired sound localization
  - dichotic speech test abnormalities with small but reliable ear asymmetries.
- These auditory deficits are associated with educational difficulties, in the absence of a close correlation between the auditory deficits and the subjects' IQ.
- Congenital aplasia or early life damage of the corpus callosum causes mild impairment of auditory interhemispheric transfer ?probably due to development of alternative pathways resulting from brain plasticity.

## The *PAX6* gene

- *PAX6* encodes a transcriptional regulator
  - Highly conserved across species
  - essential for eye and brain morphogenesis
  - Mutations of the *PAX6* associated with panocular maldevelopment including aniridia. Identification of heterozygous intragenic mutations in 80-90% of classical aniridia patients : ? *PAX6* may be the sole gene implicated in the autosomal dominant phenotype (van Heyningen , Williamson 2002).

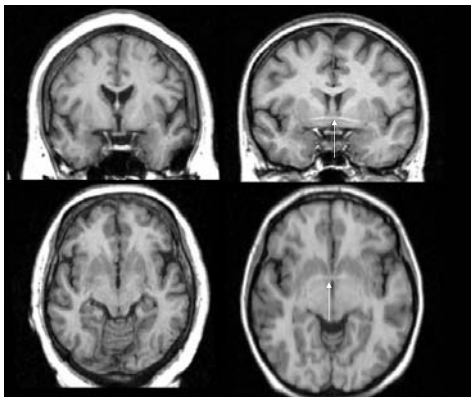
## The *PAX6* gene

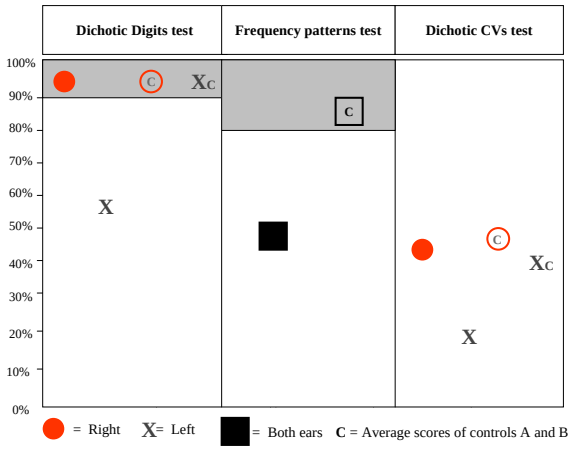
- *PAX6* and brain morphogenesis:
  - *PAX6* regulates neuronal migration, regional cortical development, early thalamocortical and corticofugal axon pathfinding (Jones et al., 2002; Talamillo et al., 2003).
  - *PAX6* mutations in humans are associated with cerebral malformations, with absence or hypoplasia of the anterior commissure and reduction in the cross-sectional area of the corpus callosum (Sisodiya et al.., 2001).

## Case report

- Heterozygous *PAX6* mutation is associated with an absent/hypoplastic anterior commissure and a reduction in the area of the corpus callosum. We found deficient auditory interhemispheric transfer in a 53 year old woman with a *PAX6* mutation who had an absent anterior commissure but normal callosal volume. This is a first report of deficient auditory hemispheric transfer in association with a *PAX6* mutation.

  *Bamiou, Musiek, Sisodiya et al., Neurology 2003*






## Conclusion from case report

- We propose that this patient's severely decreased auditory hemispheric transfer function is due to an age-related deterioration of an auditory interhemispheric pathway with a reduced capacity for plasticity/compensation, due to
  - agenesis of the anterior commissure, and/or
  - ?possible abnormalities of a normal size but functionally deficient corpus callosum.

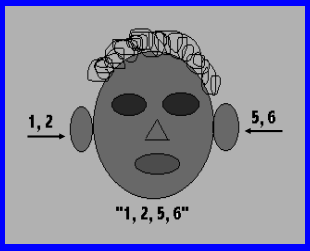
## Conclusion from case report continued

- Circumstantial evidence that an hypertrophied anterior commissure may compensate for the lack of the CC (Barr M, Corballis 2002; Fischer et al. 1992).
- This is the first case report of deficient auditory hemispheric transfer in a patient with a mutation in the *PAX6* gene.
- Further patients need to be studied

## *PAX6* - Pilot study

- We recruited 8 patients with *PAX6* mutations
- We also studied 8 age- and sex- matched controls
- Test protocol:
  - Baseline Audiometry
  - Dichotic Digits, CVs, Rhyme
  - Frequency and Duration Pattern tests
  - Gaps In Noise test

## **Dichotic Digits** (Musiek, 1983).




- •Sensitivity>70%, specificity>90%
- •Low linguistic load
- •Resistant to cochlear SNHL
- •R ear advantage

## **Dichotic CVs test** (Noffsinger et al., 1994)

- 6 digitized consonant-vowel (CV) syllables formed by combination of a stop plosive (b, p, t, d, g, k) and the vowel /a/.
- A different consonant-vowel nonsense syllable is presented to each ear, with the syllables precisely aligned in time, at 50 dBSL.
- 30 possible pairings of these syllables.
- The listener is instructed to report what he/she hears.

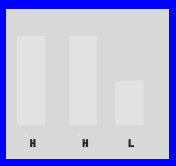
## **Dichotic Rhyme test** (Wexler and Halwes, 1983)

- 15 dichotic pairs of words that are presented twice in a 30 trial block.
- Monosyllabic consonant-vowel-consonant words that begin with one of the six stop consonants (b, p, t, d, g, k).
- The two words in each pair are matched for frequency content - difference from each other is in the initial consonant.
- The listener reports only one word.

## **Frequency /Duration Patterns** (Musiek 1994; Musiek et al., 1990)

- Three tone burst sequences of

High (1122 Hz) and low (880 Hz) tone

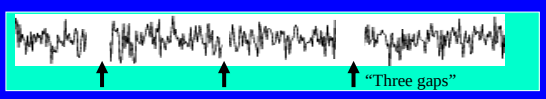




Long (500 ms) and short (250 ms) tone

- •Subject requested to label the sequence
- •Pattern recognition on R hemisphere, labelling on L hemisphere
- •Not affected by SNHL. >80% sensitivity, ~90% specificity

## Gaps In Noise test




- Monaural presentation of a 6 s white noise burst, in which 0 - 3 gaps of varying duration (2ms to 20ms) are embedded.
- Patient has to identify number of gaps in each noise burst.

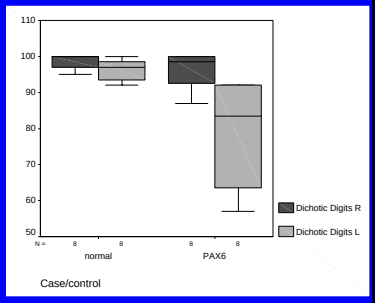
## *PAX6* -Pilot study results

| Case | Age | Mutation | Anterior commissure | Corpus callosum | DDT | FPT | DPT | Drhy* | DCV* |
|---|---|---|---|---|---|---|---|---|---|
| 4 | 30 | Premature truncation-probably haploinsufficiency | absent | normal | norm | norm | norm | abn | abn |
| 8 | 39 | In-frame deletion (predicted non-functional protein) | absent | normal | norm | abn | abn | norm | norm |
| 5 | 44 | C terminal extension | present | normal | norm | abn | abn | norm | abn |
| 2 | 40 | C terminal extension | present | small | abn | abn | norm | abn | norm |
| 1 | 53 | C terminal extension | absent | normal | abn | abn | ? | ? | abn |
| 6 | 35 | Haploinsufficiency | small | normal | abn | norm | norm | abn | abn |
| 3 | 57 | Premature truncation-probably haploinsufficiency | absent | small | abn | norm | abn | abn | abn |
| 7 | 43 | C terminal extension | absent | small | abn | norm | abn | abn | abn |

Bamiou et al., Ann Neurol 2004

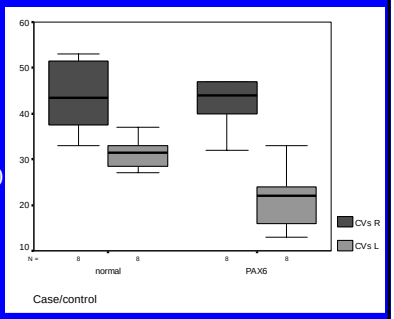
## Results – Dichotic Digits

- All the *PAX6* subjects gave normal results in the right ear.
- 5 gave abnormal results in the left ear.
- L ear scores were significantly lower in the *PAX6* group (median 83%) than in the normal group (median 97%) at p= 0.002



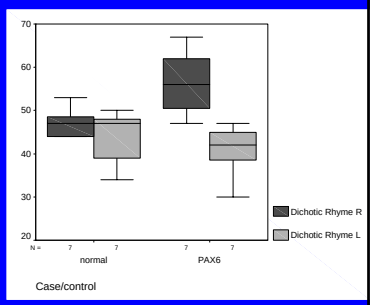

## Results –Dichotic CVs

- The R ear scores were comparable in the two groups (*PAX6* median: 44%, normal median: 43.5%).
- The L ear scores were significantly lower in the *PAX6* (median 22%) than in the normals (median 31.5%) at p= 0.005
- 5:8 *PAX6* subjects had L ear scores below the minimum value of the control group.




## Results-Dichotic Rhyme test

- The R ear score was significantly higher in the *PAX6* (median 56%) than in the normal group (median 47%) at p= 0.021.
- The L ear scores were slightly lower in the *PAX6* group (median: 42%) than in the normal group (median: 47%).
- 5:7 *PAX6* subjects had R ear scores exceeding the maximum value of the control group.




## Results: FPT, DPT, GIN

- FPT scores were abnormal in 5:8 subjects and normal in all controls.
- DPT scores were abnormal in 4:8 subjects and normal in all controls.
- Only one subject gave slightly abnormal thresholds and scores for the GIN in both ears (case 2). There was no difference in GIN thresholds or scores in either ear between the *PAX6* and the normal control group ($p>0.05$).

## Discussion

- The *PAX6* group had similar abnormalities to patients with surgical section of the corpus callosum
  - normal performance in monaural speech tests,
  - reduced to near extinct left ear performance in dichotic digits and CVs,
  - increased right ear performance in dichotic rhyme tests
  - reduced scores in the frequency and duration pattern tests

## Discussion

- These findings post callosotomy explained on the basis of three assumptions (“callosal relay model”, Zaidel 1986)
  - language perception takes place in the left hemisphere,
  - in the monaural situation both the ipsi- and contralateral pathway are functional for sound transmission, and
  - in the dichotic situation, the contralateral pathway, which dominates in auditory signal transmission, takes over.

## Other possible explanations

- "direct access model": speech stimuli from the left ear will be directly analyzed in the right auditory cortex, albeit less efficiently than in the left cortex.
- dichotic speech tasks activate a wider network in each hemisphere than simpler tasks and dichotic test results may reflect asymmetries in processing efficiency due to other "top-down" processes.
- **presence of auditory cortex or subcortical abnormalities, or diffuse abnormality of the subcortical pathways**

## Discussion

- Our results in the PAX6 group indicate the presence of deficient auditory interhemispheric transfer
- The deficient auditory interhemispheric transfer could be attributed to structural and/or functional abnormalities of the anterior commissure and corpus callosum in the *PAX6* group.

## Discussion

- Further studies of these patients would add to our understanding of the function of the commissural pathways of the brain and of the profile resulting from commissural pathway dysgenesis.
- Our unique findings broaden the possible role of *PAX6* to include higher order roles not only in visual and olfactory sensory domains, but also in auditory processing.

## 1st Paediatric Case with *PAX6* mutation

- 10 y 11 month boy
- Aniridia – *PAX6* mutation
- Son of a couple who both had *PAX6* mutations
- Parents participated in adult study
- On explanation of their test findings, the parents reported that their son had hearing difficulties

Bamiou et al., submitted

## 1st Paediatric Case with *PAX6* mutation

- Repeated pure tone audiograms have always been normal
- No past history of glue ear or ear infections. His speech and language development were age appropriate.
- He is right handed and he likes playing the trumpet. He enjoys science, maths and geography and is a bright student. He receives learning support in view of his visual difficulties.

Bamiou et al., submitted

## Paediatric Case. Symptoms

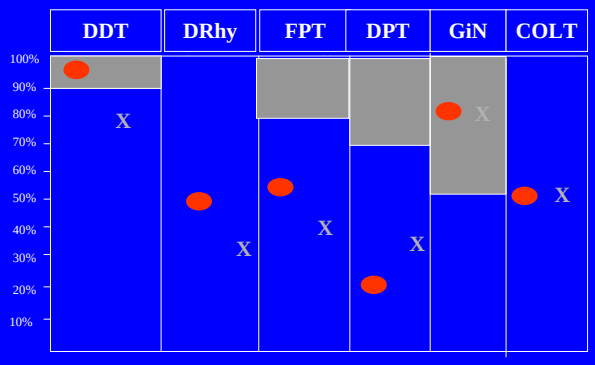
- Doing academically very well, but hearing difficulties since he started school.
- He mishears things particularly in background noise and he finds this extremely frustrating: e.g., "pigs live in a sty" versus "pigs live in the sky".
- Problems in the classroom and in the gym

Bamiou et al., submitted

## Paediatric Case. Symptoms

- Problems with sound localization : some sounds are too quick for him to be able to ascertain the location of the sound source.
- Difficulties with remembering information and instructions presented verbally
- Difficulties with prosody:
  - may misinterpret mum's tone of voice
  - may miss the joke punch-line
- Difficulty with organizational skills

Bamiou et al., submitted




OAEs – normal ABR – normal MLR – normal
Long latency potentials: immature, probably normal for his age
Bamiou et al., submitted

| CELF 4 scale/subtest | Results |
|---|---|
| Observational Rating Scale | Listening:<br>- Difficulty hearing in noisy environments<br>- Some difficulty with prosodic aspects of speech, i.e. jokes |
| | Speaking<br>- No articulation problems<br>- Occasional disfluency in speech, when under pressure |
| | Reading<br>- No difficulties reported |
| | Writing<br>- No difficulties reported |
| Word classes 2 | Receptive score:<br>- Raw score: 21<br>- Age equivalent : >16 y 11m |
| | Expressive score:<br>- Raw score: 21<br>- Age equivalent : >16y 11m |

Bamiou et al., submitted.

| CELF 4 scale/subtest | Results |
|---|---|
| Understanding Spoken Paragraphs | Raw score: 15/15<br>(C obtained the maximum possible score. The CELF 4 does not provide an age equivalent score for this subtest.) |
| Phonological awareness | Raw score: 81/85<br>Age equivalent: > 11:00 (the maximum age equivalent score provided) |
| Number repetition | Number repetition forwards:<br>- Raw score: 7<br>- Age equivalent: ± 6y 6m |
| | Number repetition backwards:<br>- Raw score: 4<br>- Age equivalent: ± 7y 11m |
| | Number repetition total:<br>- Raw score: 11<br>- Age equivalent: ± 7y 3m |

Bamiou et al., submitted

## Paediatric Case. Management

- Brain MRI (normal) – DTI
- Signal Enhancement Strategies - sound FM systems
- Auditory training:
  - Sound localization
  - Simon game
  - Targeting difficulties in background noise
- Liaison with Educational Audiologist who has already seen patient

Bamiou et al., submitted

## After the CELF assessment (performed by Dr Nicci Campbell)

- Additional support to improve his verbal working memory and organisational skills was recommended
  - whole body listening techniques
  - self-instruction and –regulation
  - recording information in pictorial form
  - mnemonic devices
  - mind-mapping and study skills
  - use of a diary
  - planning around and prioritizing deadlines.

# Paediatric PAX6 study

## Pilot study in children with *PAX6* mutations

- We recruited 11 children with aniridia from families with PAX6 mutations (age 7-17 yrs)
- 11 normal controls matched to the subjects for age- gender- and handedness

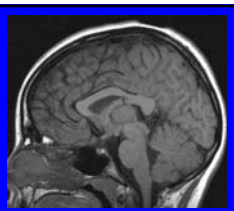
## Methods of Assessment

- Case History - Examination
- Baseline Audiologic test procedures
  - PTA, OAEs, ABR
- Behavioural central auditory tests:
  - Dichotic Digits tests, Frequency and Duration Pattern tests, Gaps in Noise test
- Brain MRI and Diffusion Tensor Imaging studies
- Questionnaire re hearing

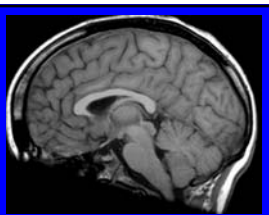
## Results

| Name | Sex | Age | Hand | Brain MRI | DDT | FPT | DPT | GiN |
|---|---|---|---|---|---|---|---|---|
| CR | M | 12 | R | normal | A | A | A | N |
| SC | F | 16 | R | small AC | N | A | A | N |
| SN | F | 14 | R | cyst in splenium | A | N | A | N |
| TN | M | 17 | R | small AC, small post CC | N | N | N | N |
| RAR | F | 7 | L | small splenium | A | | | |
| CB | F | 10 | L | Small AC, small post CC | A | A | A | N |
| GD | M | 10 | L | hypo AC, small splenium | A | A | A | N |
| RS | F | 16 | | small AC | N | A | A | N |
| FS | F | 14 | R | small AC | A | A | A | N |
| BS | F | 11 | R | small AC | A | A | A | ?A |

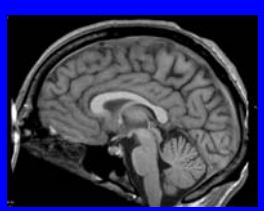
A = abnormal, N = normal, CC = Corpus Callosum, AC = Anterior Commissure



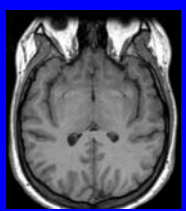
Normal (CR)



Hypoplastic AC, small splenium



Post CC< ant CC



Cyst in CC

| Name | Sex | Age | Family | Mutation | Brain MRI | DDT | FPT | DPT | GiN |
|---|---|---|---|---|---|---|---|---|---|
| *1** | *F* | *35* | *Mother of 1.1 and 1.2* | *Haplo-insufficiency R240X* | *small AC normal CC* | *A* | *N* | *N* | *N* |
| 1.1 | M | 12 | Son of 1 | *Haplo-insufficiency* | normal | A | A | A | N |
| 1.2 | F | 7 | Daughter of 1 | *Haplo-insufficiency* | small splenium | A | A | A | N |
| *2** | *F* | *44* | *Mother of 2.1* | *C terminal extension X432L* | *normal* | *N* | *A* | *A* | *N* |
| 2.1 | F | 16 | Daughter of 2 | *C terminal extension* | small AC | N | A | A | N |
| *3** | *M* | *50* | *Father of3.1 3.2* | *missence K55R* | *cyst beneath striatum* | *A* | *N* | *N* | *N* |
| 3.1 | F | 14 | Daughter of 3 | *missence* | cyst in splenium | A | N | A | N |
| 3.2 | M | 17 | Son of 3 | *missence* | small AC small post CC | N | N | N | N |
| *4** | *M* | *33* | *Father of 4.1* | *Splicing mutation* | *normal* | *N* | *N* | *N* | *N* |
| 4.1 | F | 10 | Daughter of 4 | *Splicing mutation* | small AC small post CC | A | A | A | N |
| *5** | *F* | *29* | *Mother of 5.1* | *Frameshift C47BinsCC (haplo-insufficiency)* | *absent AC* | *NT* | *NT* | *NT* | *NT* |
| 5.1 | M | 10 | Son of 5 | *Frameshift C47BinsCC (haplo-insufficiency)* | small AC small splenium | A | A | A | N |
| *6 ** | *F* | *54* | *Mother of 6.1* | *missence G36R* | *NT* | *A* | *A* | *A* | *A* |
| 6.1 | F | 16 | Daughter of 6 | *missence* | small AC | N | A | A | N |
| 7.1 | F | 14 | Sister of 7.1 | *Antistart missence (haplo-insufficiency)* | small AC | A | A | A | N |
| 7.2 | F | 11 | Sister of 7.2 | *Antistart missence (haplo-insufficiency)* | small AC | A | A | A | A |
| 8 | M | 13 | | *Inversion of chromosome 11 (haplo-insufficiency)* | NT | N | N | A | N |

## Questionnaire results

| | | No difficulties | Some difficulties | | |
|---|---|---|---|---|---|
| | | Almost always (0 points) | Frequently (1 point) | Occasionally (2 points) | Almost never (3 points) |
| understand speech in quiet* | Case | 6 | 3 | 0 | 0 |
| | Control | 9 | 0 | 0 | 0 |
| understand speech in noise | Case | 3 | 3 | 2 | 1 |
| | Control | 8 | 1 | 0 | 0 |
| understand feeling by tone of voice | Case | 5 | 2 | 2 | 0 |
| | Control | 8 | 1 | 0 | 0 |
| Understand intonation and voice inflection | Case | 4 | 3 | 2 | 0 |
| | Control | 8 | 1 | 0 | 0 |
| "get a joke" as well as his peers | Case | 4 | 4 | 1 | 0 |
| | Control | 8 | 1 | 0 | 0 |
| tell where a sound is coming from* | Case | 3 | 0 | 6 | 0 |
| | Control | 7 | 2 | 0 | 0 |

Significant differences between PAX6 children and controls, p = 0.031

## Questionnaire vs. auditory test results

- Linear regression analysis
  - the left (but not the right) dichotic digits score correlated with the reported speech-in-noise difficulties (R square = 0.371, p= 0.007).
  - Both the right and left frequency pattern scores correlated with the intonation/inflexion difficulties
    - R square = 0.308, p=0.017 for the right ear FPT score
    - R square = 0.375, p=0.004 for the left ear FPT score

## Discussion

- Difference between the paediatric and the adult cases brain MRIs :
- the AC present in 10/10 paediatric cases (smaller in 7) vs. in 4/14 adult cases (Sisodiya et al., 2001) vs. in 9/24 scanned adults (Free et al., 2003)
- ? Small samples ?
- Or age-related-degeneration of the interhemispheric structures (consistent with proposed *PAX6* maintenance function in the adult eye)

- Constellation of auditory test abnormalities in the 11 children with *PAX6* mutations , i.e.
  - the reduced left ear score in the dichotic digits test
  - bilaterally reduced scores in frequency and duration pattern tests
  - normal gaps in noise test
- Consistent with our findings in adults with *PAX6* mutations
- Similar, albeit less severe, to the test findings in patients with posterior section of the corpus callosum and splenium

## Discussion

- Deficient auditory interhemispheric transfer may underline the reported difficulties with sound localization, prosody, as well as with understanding speech in background noise.
- Acallosal subjects are reported to be less accurate than controls in localizing a moving sound (Lessard et al., 2002)
- Prosody difficulties have also been previously reported in individuals with congenital abnormalities of the interhemispheric pathway (Paul et al 2003)
- It has been suggested that the processing of speech in background noise both activates and requires input from both hemispheres, with the left hemisphere compensating for loss of phonologic information and the right hemisphere compensating for increased attention demands (Boatman et al., 2003; Scott et al., 2004)

## Speech in noise and the interhemispheric pathway

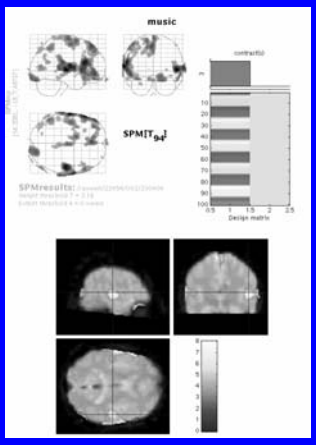
- Processing of speech in background noise activates both hemispheres.
- Oral language comprehension: integration of semantic/syntactic information (left hemisphere) with prosodic information (right hemisphere)
- Interhemispheric interaction may increase the brain's processing capacity by dividing the processing demands between the two hemispheres, in order to make maximum use of hemispheric specialization and also to facilitate processing of information in parallel.
- the interhemispheric pathway may also enhance the processing efficiency of the brain by its effect on a top-down executive function, i.e. attention.
- The left ear deficit in DDT: indirect measure of the speech in speech competition difficulties, consistent with our finding that the left ear dichotic digit test score correlated with the parent-reported speech-in-noise difficulties.

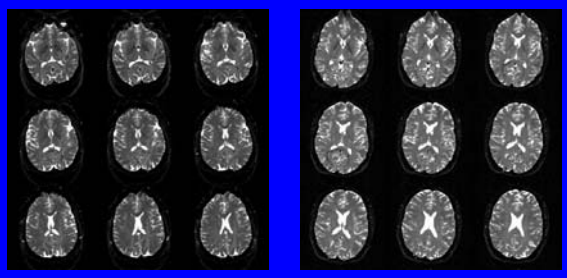
## Further studies

- Adult subjects (funded by Hearing Conservation Council):
  - more numbers – AC versus CC
  - expand test battery: localisation tasks, directed attention on dichotic tests, non-speech dichotic, electrophysiology
- Children: CAT assessment + brain MRI/DTI (funded by Sir Jules Thorn Charitable Trust).
- fMRI and Diffusion Tensor Imaging on adults

Figure 1.
Auditory fMRI for patient MR

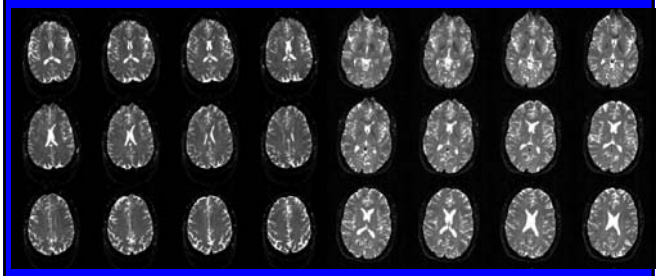
Courtesy of Dr Rob Powell



Seed point in splenium of callosum MR (left) and control (right)
Note false positive connections to the lateral temporal lobe in both.

Courtesy of Dr Rob Powell



Anterior corpus callosum – MR (left) and control (right)
(seed point placed in 6th image)

Courtesy of Dr Rob Powell

## CC and AC may

- Reinforce tonotopicity
- subserve both binaurality and sound localisation
- connecting maps are reweighted and input may be transferred to specific cortical sites.
- temporal transformation of neural transmission, (synchronisation or desynchroniation of neural activity)

## Some final points to discuss and think about

- Integration subtype of APD
- APD in the older population: role of interhemispheric pathway
- Audition and the interhemispheric pathway in Alzheimer
- Maturation and plasticity

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