

1. Introduction

Temporal processing (TP) on a timescale of tens to hundreds of milliseconds (msec) is required to implement a range of perceptual and cognitive tasks where precise registration of time-varying information within and between stimulus sequences is required.

Impairments in TP have been associated with a number of neuro-biologically based developmental disorders, including dyslexia¹, specific language impairment², and ADHD³.

Psychophysical and neurophysiological measures of TP may be useful in understanding the mechanistic overlap between disorder phenotypes.

The clinical potential of TP measures depends on developing assessment protocols that yield reliable and valid data in the shortest times possible for use in populations who may not be fully compliant or otherwise unable to endure extended recording sessions.

Auditory Gap detection (GD) provides a 'pure' measure of TP. It measures the length of the very shortest event (a silent gap in noise) that can be discerned by the auditory system; an index of neural time resolution.

Normal gap sensitivity has been well established psychophysically^{4,5} and using magnetoencephalography (MEG)^{6,7}, in adults. Absolute thresholds for GD measured psychophysically can reach 2-3 ms, but are subject to large inter-individual differences.

2. Aims

1. Investigate whether a deficit in temporal processing, measured using traditional auditory gap detection, is a potential endophenotype for developmental disorders.
2. Develop an optimised magnetoencephalography paradigm for use with young children and patient populations, where full compliance and vigilance for a neuroimaging task may not be assured.

3. Methods

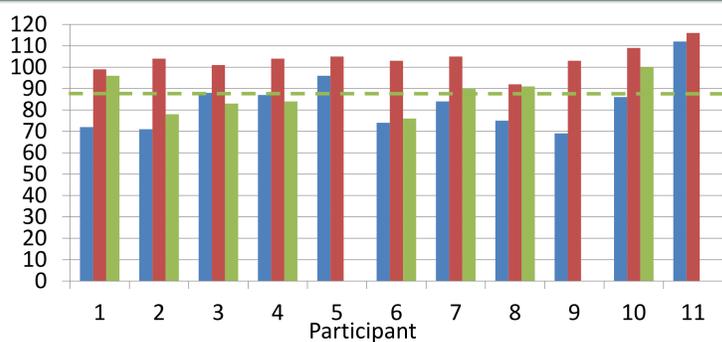
Participants

- 11 children (9 male) Average age: 10y 4 m (8y 11m to 11y 7ms (sd 8m)
- Average or above intelligence (FSIQ >85)
- Mixed ability group referred to clinic for specific learning difficulties (see Box 4)

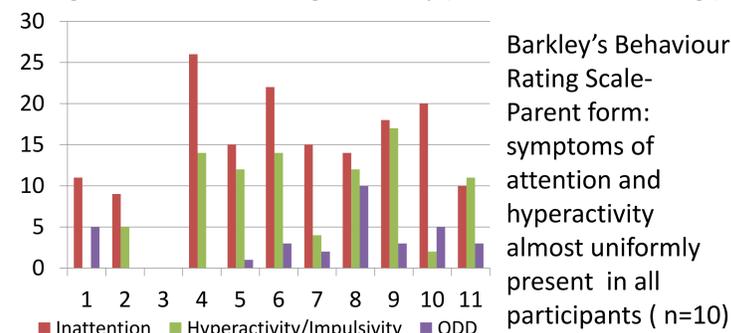
Assessments

- Wechsler's Intelligence Scales for Children – 3rd/4th Edition
- Berkley's Behavior Rating Scale – Parent form
- Test of Word Reading Efficiency (TOWRE)
- Comprehensive test of phonological processing (C-TOPP)
- Psychophysical auditory gap detection task
- Novel MEG auditory gap detection paradigm

4. Participant profiles



1. Actual WIAT-II Word Reading Score vs. predicting Word Reading Score using WISC Verbal Comprehension Index
2. E.g. Phonemic Decoding Efficiency (TOWRE; <90= Low avg.)

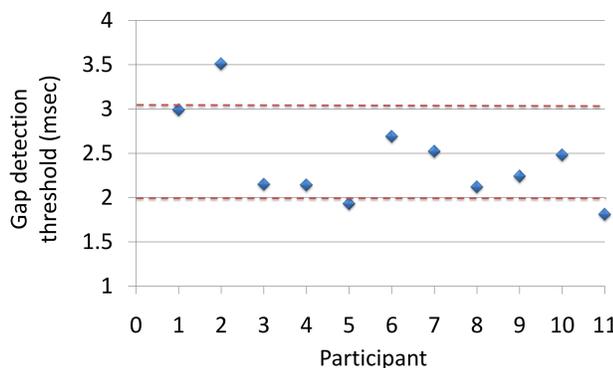


Barkley's Behaviour Rating Scale-Parent form: symptoms of attention and hyperactivity almost uniformly present in all participants (n=10)

5. Psychophysical gap detection

2 forced-choice 2-down, 1-up adaptive staircase method⁸

- Binaural 70dB SPL presentation over calibrated Sennheiser HD480s
- Gap centred in 500msec diotic Gaussian noise
- Initial 30msec gap length with a step size of 1.2
- Targets threshold corresponding to 70.7% correct responses
- Thresholds calculated using geometric mean of last 8 reversals



No deficit in auditory gap detection observed: Mean GD threshold = 2.42msec (sd .55; n=11).

4 participants completed task twice for reliability measure; CoV= 5.8%.

Using a similar paradigm, Ingelghem et al. (2001)⁹ observed a GD threshold of 2.7msec in 10 controls (mean age 11 years), but significantly lower threshold in 10 dyslexic children (3.3msec, sd= .5).

Rigorous, well controlled psychophysical measures are lengthy and repetitive and may be inappropriate for children. Results can be confounded by high 'workload' (attention, concentration, motivation), the response criteria used and use of abstract responses (e.g. button press).

Diedler et al.⁴ reported a failure to obtain psychophysical thresholds on nearly one-third of a group of 43 children with language difficulties.

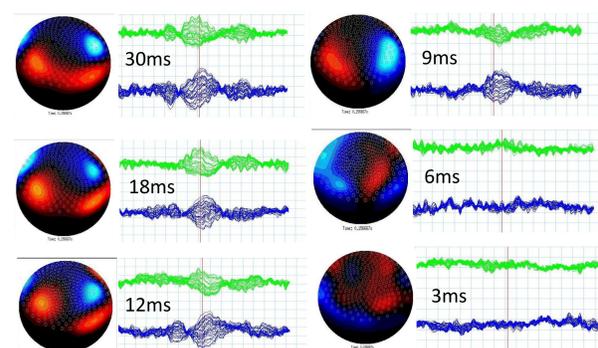


6. Magnetoencephalography (MEG) measures of Gap Detection

Magnetoencephalography is a non-invasive neuroimaging tool for mapping brain activity by recording magnetic fields produced by brain activity.

Advantages of using MEG to study GD measures of temporal processing:

- Passive - Removes all attention /concentration-related confounds
- Working Memory confounds are minimised
- Safe for repeated paediatric use
- Temporal processing measured at the perceptual, neural level
- Millisecond temporal precision
- Allows accurate localisation of activity



Auditory evoked potentials and field Patterns for N100m response (Male, 10). Left temporal channels in green, right channels in blue. Field patterns show magnetic dipoles localising activity to temporal cortex.

Novel auditory gap detection stimuli with MEG:

- 340sec continuous diotic Gaussian noise
- Pseudo-randomised gaps of 3, 6, 9, 12, 18 or 30msec, jittered around 500msec intervals

80 500msec epochs for each gap duration averaged to produce auditory evoked potential.

Response strength directly related to gap duration, with very little response at shortest gaps (see example data from one participant (#5), left).

Gradient of linear relationship between averaged response amplitude and gap length provides a sensitive metric of temporal processing.



MEG data were collected using an 252 channel CTF scanner, purpose built for adults (see photograph above). The Aston Brain Centre is the first centre in Europe to develop a paediatric-compliant MEG system and facility for the study of brain development in children.

7. Conclusions

1. No deficits in temporal discrimination, indexed by auditory GD, in a group of mixed ability children with specific learning difficulties.
2. Reliable measures of auditory cortical responses obtained in 10/11 children using novel, short (<6 mins) MEG recordings.
3. MEG was well tolerated by children, despite ADHD symptomatology, highlighting its potential utility for use in non-compliant and clinical populations.
4. Neural level measures of GD can be used to cross-validate results obtained from psychophysical data.
5. MEG data needs to be validated using larger clinical groups, alongside normative data from typically developing children.

8. References

- [1] Farmer, M. E. & Klein, R. M. (1995). *Psychon Bull & Rev*, 2, 460. [2] Shanahan, M, et al. (2006). *J. Abnorm. Child Psychol.*, 34, 585. [3] Miller, C.A. et al. (2001). *J Speech Lang Hearing Res*, 44, 416. [4] Diedler, J. et al., (2009). *Neuroreport*, 20, 844. [5] Moore, B.C. (1993). *Ann. N.Y. Acad. Sci.*, 682, 119. [6] Shemesh, R. (2008). *J. Basic Clin Physiol Pharmacol*, 19, 249. [7] Gage, N., Roberts, T.P.L & Hickok, G. (2006). *Brain Research*, 1069, 166. [8] Levitt, H. (1971). *J Acoust Soc Am*. 49, 2, Suppl 2:467+. [9] Van Ingelghem et al. (2001). https://perswww.kuleuven.be/~u0032380/papers/VanIngelghem_StudiaPaedag.pdf

9. Acknowledgements

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