Speech perception ability in individuals with Friedreich ataxia

Gary Rance,1 Rosanne Fava,2 Heath Baldock,1 April Chong,1 Elizabeth Barker,1 Louise Corben3 and Martin B. Delatycki3

1Department of Otolaryngology, The University of Melbourne, East Melbourne 3002, Australia, 2Royal Victorian Eye & Ear Hospital and 3Murdoch Childrens Research Institute, Melbourne, Australia

Correspondence to: Assoc Prof. Gary Rance, PhD, Department of Otolaryngology, The University of Melbourne, 172 Victoria Parade, East Melbourne 3002, Australia
E-mail: grance@unimelb.edu.au

The aim of this study was to investigate auditory pathway function and speech perception ability in individuals with Friedreich ataxia (FRDA). Ten subjects confirmed by genetic testing as being homozygous for a GAA expansion in intron 1 of the \( \text{FXN} \) gene were included. While each of the subjects demonstrated normal, or near normal sound detection, 3 of the 10 showed electrophysiological evidence of auditory pathway disorder [presenting with the auditory neuropathy/dyssynchrony (AN/AD) result pattern], and 9 of the 10 showed abnormal speech understanding when tested with levels of background noise typical of everyday listening conditions.

Information transmission analyses of the speech perception findings for the three FRDA subjects with AN/AD type hearing loss when compared with those of a cohort of individuals with peripheral [sensorineural (SN)] hearing loss, showed a distinct pattern of perceptual disruption. Where the listeners with SN loss confused sounds on the basis of frequency (pitch) differences, the FRDA subjects with AN/AD made errors that reflected an inability to perceive temporal (timing) cues in the speech sounds.

Keywords: Friedreich ataxia; auditory; speech perception

Abbreviations: ABR = auditory brainstem response; AN/AD = auditory neuropathy/dyssynchrony; FRDA = Friedreich ataxia; SN = sensorineural; SNR = signal-to-noise ratio


Introduction

Friedreich ataxia (FRDA) is the commonest inherited ataxia (Vonken et al., 2004). It is characterized by progressive limb and trunk ataxia, hypertrophic cardiomyopathy, scoliosis and an increased rate of diabetes mellitus. Lifespan is reduced with the average time from onset to death being 36 years (de Michelle et al., 1996). FRDA is due to mutations in the \( \text{FXN} \) gene [previously called X25 and FRDA] (Campuzano et al., 1996). About 98% of mutant alleles have an expanded GAA trinucleotide repeat in intron 1 of the gene. The other 2% are point mutations (Cossee et al., 1999).

Hearing loss (as measured by the behavioural audiogram) is one of the less frequent symptoms in individuals with FRDA (Lynch et al., 2002). Elevated hearing levels (impaired detection of sound at low levels) have been reported at rates ranging from 8% to 13% (Harding, 1981; Durr et al., 1996). This prevalence level is, however, somewhat higher than would be expected for the general population where permanent hearing loss is thought to affect <4% of adults in the 15–50 year age range (Wilson et al., 1999).

In addition to hearing difficulties related to decreased detection of sound, individuals with FRDA can also present with disorder affecting neural conduction in the central auditory pathways (Satya-Murti et al., 1980; Jabbari et al., 1983; Starr et al., 1996; Lopez-Diaz-de-Leon et al., 2003). Individuals with FRDA with this form of hearing loss, often termed ‘auditory neuropathy/dys-synchrony’ (Starr et al., 1996; Berlin et al., 2001), typically show absent or distorted responses from the cochlear nerve and auditory brainstem (Satya-Murti et al., 1980; Jabbari et al., 1983) and yet demonstrate normal pre-neural responses from the cochlear outer hair cells such as otoacoustic emissions (OAEs) and cochlear microphonics (CMs) (Starr et al., 1996; Sininger and Oba, 2001; Lopez-Diaz-de-Leon et al., 2003). This result pattern is consistent with histological evidence from the temporal bones of FRDA individuals that has shown
selective damage to cochlear nerves in conjunction with preserved cochlear structures such as the organ of corti and hair cells (Spoendlin, 1974).

The auditory brainstem response (ABR) is a series of evoked potentials arising from auditory pathway activity in the first 15 ms after the presentation of an abrupt auditory stimulus. The response can only occur in the auditory pathway if the stimulus sound has exceeded the subjects’ hearing threshold, and hence by varying the stimulus presentation level, ABR testing can be used to estimate sound detection threshold in subjects with normal function or peripheral hearing loss. An inability to record this response in patients with FRDA, however, does not necessarily reflect impaired hearing sensitivity, but may suggest an abnormality in neural conduction in the auditory pathway. This may be the result of either a paucity of neural elements available to contribute to the volume-conducted response, or a disruption of the synchrony or timing of neural activity in the auditory brainstem (Starr et al., 1996). In the former case, neuronal degeneration with axonal or dendritic loss may mean that the potentials generated in the auditory pathway are simply too small to be recorded by scalp-sited electrodes. In the latter, the remaining fibres may have altered nerve conduction making the ABR unrecognizable not because of a lack of activity, but because the timing of that activity is not sufficiently precise to allow extraction from within the EEG using signal averaging procedures (Clarke et al., 1961). As variations in the timing of responses to individual stimuli of only fractions of a millisecond are sufficient to disrupt the averaged ABR, it has been suggested that ‘temporal inconsistency’ may be a factor in patients with the AN/AD result pattern (Starr et al., 1991; Kraus et al., 2000; Michalewski et al., 2005).

The perceptual effects of auditory pathway disorder have not been specifically investigated in patients with FRDA, but the consequences of this form of hearing loss have been considered in the broader population of individuals with AN/AD. This group in fact shows a pattern of perceptual disruption quite different from that seen for ears with cochlear or ‘sensorineural’ type hearing loss. As the cochlea is responsible for the initial processing of spectral information, insult in this area typically results in a loss of ‘frequency resolution’, the ability to perceive different frequency components within a complex signal (Moore, 1995) and ‘frequency discrimination’, the ability to judge the pitch of auditory stimuli (Moore, 1973; Sek and Moore, 1995).

In contrast, AN/AD type hearing loss in disrupting the timing of neural signals in the auditory pathway, tends to impair aspects of auditory perception based on temporal cues (Zeng et al., 1999; Rance et al., 2004). Affected ears for example, struggle to track rapidly occurring changes in the level or frequency of auditory signals. Furthermore, the severity of the temporal abnormality in these subjects is strongly related to their ability to understand speech (Rance et al., 2004; Zeng et al., 2005).

Speech perception problems have been a consistently reported consequence of AN/AD type hearing loss. Severe difficulties have been shown in subjects with abnormal audiograms (where performance levels are typically far worse than expected for ears with SN hearing loss of equivalent degree) and even in subjects who show the AN/AD result pattern in conjunction with normal hearing thresholds (Starr et al., 1996, 2000; Zeng et al., 2001; Rance et al., 2002). As such, it is the degree of signal distortion rather than the audibility of speech sounds that determines perceptual ability.

As well as showing problems with speech understanding in favourable (quiet) listening conditions, extreme difficulties in background noise have been reported in adult subjects with AN/AD (Starr et al., 1998; Kraus et al., 2000; Shallop, 2002; Zeng and Liu, 2006). Each of these studies has presented cases showing essentially normal speech perception in quiet, but little or no speech understanding at signal-to-noise ratios (SNR) consistent with everyday listening conditions.

The primary aim of this study was to investigate speech perception abilities in subjects with FRDA. Part A of the study examined the effects of background noise on overall speech understanding, comparing the results from FRDA patients with a control group of healthy subjects with similar (normal) hearing levels. Part B looked in detail at the pattern of perceptual errors made by the FRDA patients who presented with the AN/AD result pattern. In this experiment, the findings were compared with those of ears with SN type hearing loss.

**Methods**

**Subjects**

Invitations to participate in the study were sent to all people with FRDA in the state of Victoria known to the research team at the Murdoch Childrens Research Institute. As testing took place at the subject’s home, participation was subsequently restricted to those residing within 2 h drive of the University of Melbourne. Ten individuals confirmed by genetic testing as being homozygous for a GAA expansion in intron 1 of the FXN gene were included in the study. There were five male and five female subjects aged between 17 and 51 years (35.4 ± 10.6 years). Patient details for these subjects can be seen in Table 1. Included is each individual’s score for a measure of disease severity, the Friedreich Ataxia Rating Scale (FARS) (Subramony et al., 2005) administered within 6 months of the audiological examination. The FARS comprises a measure of ataxia, activities of daily living and a neurological subscale, which includes measures of bulbar function, upper and lower limb coordination and peripheral sensory function (Fahey et al., 2007). The FARS is scored out of 167, a higher score indicating greater level of functional disability.

Nine of the 10 subjects with FRDA had undergone visual assessment (Sloan Low Contrast Letter Chart) within 6 months of the audiological assessment and all were found to have normal acuity. The final subject (FRDA10) also showed normal function when last tested (12 months prior to the current study). In contrast, 6 of the 10 subjects with FRDA were included in...
a recent study of vestibular function (Fahey et al., 2008) and all showed abnormalities in vestibulo-ocular reflex latency and gain.

Each subject underwent audiometric assessment using ER-4 insert phones and a portable audiometer in a quiet room where background noise levels were <40 dBA. Hearing thresholds at octave frequencies across the audiometric range (250 Hz–8 kHz) were established in each ear. The fact that the test environments were not sound-proofed raises the possibility of audiometric threshold elevation, but 9 of the 10 subjects still showed hearing levels within the normal range, and the one subject with elevated thresholds (FRDA10), showed only mild degree hearing loss in one ear (see Table 1 for details).

In each individual, the ear with the poorer audiometric thresholds then underwent transient otacoustic emissions, auditory evoked potential and speech perception assessment. Otacoustic emissions were recorded using a Madsen Capella Cochlear Emissions Analyzer. Responses were considered present when the waveform repeatability was >50% and when the response amplitude exceeded the noise spectrum by >6 dB in at least three frequency bands. Each of the FRDA subjects showed repeatable emissions indicating normal peripheral (middle ear and cochlear outer hair cell) function.

ABR testing was carried out using the AUDERA evoked potential system. The stimuli were acoustic clicks (100 µs duration) presented via an ER-4 insert phone. Presentation rate was 33.1 Hz and responses from 2000 stimuli were averaged to produce each test run.

Repeateable scalp potentials to stimuli presented at 90 dBnHL were recorded in 7 of the 10 FRDA subjects. The remaining three subjects (FRDA8-10) all fit the AN/AD result pattern in that they showed abnormal ABR response to clicks at maximum presentation levels (wave I present only), and yet showed clear pre-neural responses (cochlear microphonics and otacoustic emissions).

In addition to the FRDA subjects, 30 adults with normal medical and otological histories were assessed. The mean age for this control cohort was 34.9 ± 10.9 years and each subject had audiometric thresholds of <10 dBHL at frequencies across the audiometric range in the ear that underwent speech perception assessment.

ABR response testing was carried out using assessment techniques identical to those employed with the FRDA group. Repeatable potentials were obtained in all cases to acoustic clicks at 90 dBnHL. A response waveform for an individual typical of this control cohort (N21) can be seen in Fig. 1. Also shown are responses from an FRDA subject with ABR present (FRDA3) and an FRDA subject without ABR (FRDA8). This latter example illustrates the AN/AD result pattern showing phase-related cochlear microphonic responses to both rarefaction and compression stimuli, with absent responses from the central auditory brainstem.

ABR latencies and amplitudes for each of the FRDA subjects are shown in Table 2. Also shown are the group mean results for the normal cohort. Absolute and interpeak latencies for the FRDA subjects who had ABRs (FRDA1-7) were virtually identical to those obtained for the control subjects indicating normal conduction speed in the ABR. There was also no difference between the wave I response amplitudes of the two groups. However, wave V amplitudes were significantly smaller in the FRDA with ABR cohort, perhaps reflecting a reduced number of neural elements in the central auditory pathways of these subjects. This result is

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**Table 1** FRDA subject details

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age at onset (years)</th>
<th>GAA repeats</th>
<th>FARS</th>
<th>Age at assess. (years)</th>
<th>Ear tested</th>
<th>Hearing level (dBHL)</th>
<th>Acoustic reflex (Av. dB)</th>
<th>ABR</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRDA1</td>
<td>F</td>
<td>18</td>
<td>447</td>
<td>99</td>
<td>25</td>
<td>Left</td>
<td>17</td>
<td>90</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA2</td>
<td>M</td>
<td>28</td>
<td>606</td>
<td>106</td>
<td>48</td>
<td>Right</td>
<td>13</td>
<td>95</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA3</td>
<td>M</td>
<td>21</td>
<td>527</td>
<td>62.5</td>
<td>30</td>
<td>Left</td>
<td>10</td>
<td>95</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA4</td>
<td>F</td>
<td>16</td>
<td>630</td>
<td>111.5</td>
<td>51</td>
<td>Right</td>
<td>18</td>
<td>95</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA5</td>
<td>M</td>
<td>26</td>
<td>560</td>
<td>80</td>
<td>43</td>
<td>Right</td>
<td>20</td>
<td>105</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA6</td>
<td>F</td>
<td>14</td>
<td>780</td>
<td>95.5</td>
<td>29</td>
<td>Right</td>
<td>7</td>
<td>90</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA7</td>
<td>M</td>
<td>14</td>
<td>569</td>
<td>65.5</td>
<td>17</td>
<td>Left</td>
<td>10</td>
<td>95</td>
<td>Present</td>
</tr>
<tr>
<td>FRDA8</td>
<td>F</td>
<td>8</td>
<td>642</td>
<td>124</td>
<td>33</td>
<td>Left</td>
<td>20</td>
<td>NR (105)</td>
<td>Absent</td>
</tr>
<tr>
<td>FRDA9</td>
<td>F</td>
<td>10</td>
<td>706</td>
<td>115</td>
<td>40</td>
<td>Left</td>
<td>20</td>
<td>NR (105)</td>
<td>Absent</td>
</tr>
<tr>
<td>FRDA10</td>
<td>M</td>
<td>14</td>
<td>656</td>
<td>119</td>
<td>38</td>
<td>Left</td>
<td>27</td>
<td>105+</td>
<td>Absent</td>
</tr>
</tbody>
</table>

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**Fig. 1** ABR recordings for three subjects to acoustic-clicks presented at 90 dBnHL. The top three tracing pairs show responses to rarefaction stimuli and the bottom tracings were obtained to compression stimuli. The top tracings show responses from a subject typical of the normal cohort (N21). ABR waves I, III and V are noted. The second tracing pair shows ABRs obtained from an individual with FRDA3. The bottom two tracing pairs were obtained from subject FRDA8. In this subject, the ABR is absent but the cochlear microphonic response (the positive peaks of which are represented by asterisks) is present.
consistent with the findings of previous studies indicating axonal degeneration in the sensory nerves of individuals with FRDA (Hughes et al., 1968; Nolano et al., 2001).

**Apparatus and procedures**

**Part A**

Both open- and closed-set speech perception assessment was carried out for each subject. Evaluation was typically completed in one 45 min session but some subjects required a number of rest periods to maintain optimal concentration. The test stimuli and competing noise signals for both experiments were presented ipsilaterally via ER-4 insert phones. Stimulus calibration was carried out using a Bruel & Kjaer Type 1625 sound level meter attached to a Type 4157 ear simulator.

**Closed set speech perception.** Adaptive Spondees in noise (ADSPON) is a closed-set speech perception task that requires that the subject select from a set of four spondees represented by pictures displayed on a computer monitor. (A ‘spondee’ is a bi-syllabic word with equal stress on each syllable.) The subject can make their selection either by repeating the test word, or pointing to one of the images. The recorded test stimuli were held constant at 70 dBSPL in the presence of varying levels of background noise, and the SNR at which the listener could correctly identify the spondees 79.4% of the time was determined (Rance et al., 2007).

**Open set speech perception.** The stimuli in this case were recorded consonant-nucleus-consonant (CNC) words phonemically balanced to Australian English and presented to the test ear at 65 dBSPL (RMS). The competing noise was continuous 4-talker babble. A CNC word list, consisting of 50 words, was presented in each of four listening conditions: quiet (no competing signal) and speech in noise presented at 0, +5, +10 dB S/N ratios. For analysis purposes the ‘quiet’ condition was assigned a S/N ratio of +20 dB reflecting the typical relation between the stimulus and background noise levels in the test environment. Subject responses were phonetically transcribed in real-time and a ‘percentage phonemes correct’ score was generated for each listening condition.

**Table 2** ABR findings to rarefaction clicks presented at 90 dBnHL

<table>
<thead>
<tr>
<th>Subject</th>
<th>Latency wave I</th>
<th>Latency wave III</th>
<th>Latency wave V</th>
<th>Interpeak latency I–V</th>
<th>Interpeak latency I–III</th>
<th>Interpeak latency III–V</th>
<th>Amplitude wave I</th>
<th>Amplitude wave V</th>
<th>Amplitude V/I ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRDA1</td>
<td>1.38</td>
<td>3.50</td>
<td>5.38</td>
<td>4.00</td>
<td>2.12</td>
<td>1.88</td>
<td>0.23</td>
<td>0.27</td>
<td>1.18</td>
</tr>
<tr>
<td>FRDA2</td>
<td>1.54</td>
<td>3.71</td>
<td>5.63</td>
<td>4.08</td>
<td>2.17</td>
<td>1.92</td>
<td>0.12</td>
<td>0.12</td>
<td>1.00</td>
</tr>
<tr>
<td>FRDA3</td>
<td>1.59</td>
<td>3.88</td>
<td>5.54</td>
<td>3.96</td>
<td>2.29</td>
<td>1.67</td>
<td>0.18</td>
<td>0.17</td>
<td>0.97</td>
</tr>
<tr>
<td>FRDA4</td>
<td>1.38</td>
<td>3.63</td>
<td>5.46</td>
<td>4.08</td>
<td>2.25</td>
<td>1.83</td>
<td>0.34</td>
<td>0.4</td>
<td>1.12</td>
</tr>
<tr>
<td>FRDA5</td>
<td>1.50</td>
<td>3.63</td>
<td>5.42</td>
<td>3.92</td>
<td>2.13</td>
<td>1.79</td>
<td>0.19</td>
<td>0.19</td>
<td>0.62</td>
</tr>
<tr>
<td>FRDA6</td>
<td>1.54</td>
<td>3.54</td>
<td>5.46</td>
<td>3.92</td>
<td>2.00</td>
<td>1.92</td>
<td>0.40</td>
<td>0.36</td>
<td>0.91</td>
</tr>
<tr>
<td>FRDA7</td>
<td>1.50</td>
<td>3.63</td>
<td>5.42</td>
<td>3.92</td>
<td>2.13</td>
<td>1.79</td>
<td>0.19</td>
<td>0.33</td>
<td>1.74</td>
</tr>
<tr>
<td>FRDA8</td>
<td>1.70</td>
<td></td>
<td>5.34</td>
<td></td>
<td></td>
<td></td>
<td>0.30</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>FRDA9</td>
<td>1.68</td>
<td></td>
<td>5.46</td>
<td></td>
<td></td>
<td></td>
<td>0.28</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>FRDA10</td>
<td>1.65</td>
<td></td>
<td>5.46</td>
<td></td>
<td></td>
<td></td>
<td>0.17</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>FRDA mean (SD)</td>
<td>1.54 (0.11)</td>
<td>3.65 (0.13)</td>
<td>5.47 (0.08)</td>
<td>3.98 (0.07)</td>
<td>2.16 (0.10)</td>
<td>1.83 (0.09)</td>
<td>0.24 (0.10)</td>
<td>0.25 (0.12)</td>
<td>1.09 (0.35)</td>
</tr>
<tr>
<td>Normal mean (SD)</td>
<td>1.45 (0.16)</td>
<td>3.55 (0.18)</td>
<td>5.45 (0.17)</td>
<td>4.00 (0.16)</td>
<td>2.10 (0.13)</td>
<td>1.91 (0.13)</td>
<td>0.27 (0.11)</td>
<td>0.46 (0.12)</td>
<td>1.93 (0.79)</td>
</tr>
<tr>
<td>FRDA versus Normal</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &gt; 0.05</td>
<td>P &lt; 0.01</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Response latencies are expressed in milliseconds (ms) and amplitudes are expressed in microvolts (µV). Wave absence.

**Part B**

In order to better understand the perceptual difficulties faced by the FRDA subjects with AN/AD-type hearing loss, a more detailed speech perception evaluation was carried out for the three AN/AD cases. Each ear was assessed (n = 6) using four lists of CNC stimuli (200 words) presented at the +10 dB signal to noise ratio (Evoked potential assessment of the second ear in these subjects was undertaken. In each case, absent ABR and present cochlear microphonic/OAE responses were obtained confirming the presence of AN/AD-type hearing loss bilaterally). The subjects’ responses in this phase of the study were scored live, and were also recorded on high quality video for off-line phonetic transcription.

As the speech perception experiment required that each subject repeat a series of stimulus words, and as speech intelligibility problems (such as dysarthria) have been noted in patients with FRDA (Blaney and Hewlett, 2007), a phonetic profile was obtained for each of the AN/AD subjects using a modified version of the ‘Articulation Survey’ (Atkin and Fisher, 1996). Subjects were required to read, at a comfortable pace, each word on the ‘Articulation Survey Response Sheet’, thus eliciting each target phoneme in the word initial, medial and final position. Target phonemes (the 24 consonants used in Australian English) were recorded as either acquired or absent in each word position.

Overall, the Articulation Survey revealed very few speech production errors. Subject FRDA8 mis-produced 3 of the 64 targets, Subject FRDA10 made only two errors and Subject FRDA9 correctly produced all of the target phonemes in each word position. Furthermore, the articulation errors that were observed were not consistent between subjects and did not fit the pattern of errors considered by Blaney and Hewlett (2007) to be typical of FRDA subjects with dysarthria. Each of our subjects for example, showed a full stop consonant (/p/, /b/, /t/, /d/, /k/, /g/) repertoire. As such, errors made by these subjects during speech perception assessment were assumed to reflect their hearing (rather than speech production) difficulties.

A control group of three subjects with SN-type hearing loss also underwent the speech perception assessment. These subjects, aged between 56 and 67 years, were selected to match the overall phoneme correct scores (obtained in study Part A) for the FRDA subjects with AN/AD (at the +10 dB S/N ratio). Mean CNC
phoneme scores for the AN/AD group ranged from 33% to 64% (median: 46%) and for the SN group ranged from 34% to 65% (median: 44%). Patient details for the AN/AD and control subjects are shown in Table 3. The behavioural audiograms of the SN subjects were all in the moderate hearing loss range, apart from the right ear for subject SN3, which showed essentially normal hearing. Speech perception testing for this ear subsequently revealed too few errors to allow valid comparison with the AN/AD group so the findings were excluded. The average hearing level for the five remaining SN ears was 59.8 ± 7.0 dB. As such, assessment required a higher stimulus presentation level [max: 105 dBSPL (RMS)] than was used for the AN/AD cohort. In each case, the SN subjects presented with relatively flat audiograms with the worst-test frequency (typically 4 kHz) showing an audiometric threshold of ≤70 dBHL. The full range of speech sounds should, therefore, have been audible at the test presentation level.

The phonetically transcribed data from the CNC speech perception assessment for each subject was subjected to an ‘information transmission analysis’ (Miller and Nicely, 1955) using the Infotransmit® software program. Information transmission measures the covariance between input (phoneme stimulus) and output (subject response) allowing a detailed investigation taking into account not only the correct responses, but also the pattern of mistakes. As such, it can provide an indication not only of a listener’s overall degree of perceptual deficit, but of the specific phoneme errors that s/he is making.

Results

Part I—speech perception in noise

Closed-set speech perception in noise

Results of the ADSPON speech perception task showed significant differences between subject groups. The mean SNR required to correctly identify spondee stimuli (79.4% of the time) for the normally hearing cohort was −12.6 ± 1.6 dB, whereas for the FRDA group without AN/AD the criterion was reached at −8.1 ± 5.0 dB and the FRDA group with AN/AD was −1.3 ± 4.1 dB. A one-way analysis of variance showed a significant group effect \( F_{(2,37)} = 30.0, P < 0.001 \). Post hoc analysis (Tukey) revealed that the normal hearing control subjects could cope with significantly lower S/N ratios than both the FRDA cohorts and that the group with AN/AD was significantly poorer in background noise than the FRDA group without AN/AD.

Regression analyses (Pearson r) for the 10 FRDA subjects showed no correlation between ADSPON SNR and age at disease onset \( (P = 0.694) \), disease duration \( (P = 0.367) \), GAA1 repeat size \( (P = 0.793) \) and FARS score \( (P = 0.554) \).

Open-set listening in noise

Group results. Findings for the CNC word speech perception test revealed clear differences between subject groups. Subject group and S/N ratio differences were analysed using a two-way analysis of variance employing a general linear model to account for the different subject numbers in each group (unbalanced design). CNC phoneme scores were significantly related to both subject group \( F_{(2,148)} = 410.7, P < 0.001 \) and S/N ratio \( F_{(2,148)} = 209.3, P < 0.001 \). Furthermore, a significant interaction between subject group and S/N ratio was obtained indicating that the effect of noise on perceptual ability was not equal across subject groups \( F_{(6,148)} = 15.7, P < 0.001 \). Mean CNC phoneme scores for each listening condition and each group are shown in Table 4. Also shown are the mean scores for each S/N ratio (across all of the subjects) and scores for each group (across all of the listening conditions).

Analysis of variance showed significant group effects at each of the listening conditions [+20 dB: \( F(2,37) = 37.9, P > 0.001 \); +10 dB: \( F(2,37) = 112.3, P > 0.001 \); +5 dB: \( F(2,37) = 142.9, P > 0.001 \); +0 dB: \( F(2,37) = 123.0, P > 0.001 \)].

Table 3 | Three-frequency average hearing level and open set speech perception scores (Averaged over four lists of CNC words) for subjects with AN/AD and SN type hearing loss

<table>
<thead>
<tr>
<th>Subject</th>
<th>Aetiology</th>
<th>Ear</th>
<th>Av. Hearing level (dBHL)</th>
<th>CNC phoneme score (%) (+10 dB S/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRDA8</td>
<td>AN/AD</td>
<td>Left</td>
<td>20</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>18</td>
<td>46</td>
</tr>
<tr>
<td>FRDA9</td>
<td>AN/AD</td>
<td>Left</td>
<td>20</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td>FRDA10</td>
<td>AN/AD</td>
<td>Left</td>
<td>27</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>20</td>
<td>37</td>
</tr>
<tr>
<td>SN1</td>
<td>Presbyacusis</td>
<td>Left</td>
<td>55</td>
<td>56</td>
</tr>
<tr>
<td>SN2</td>
<td>Presbyacusis</td>
<td>Left</td>
<td>53</td>
<td>65</td>
</tr>
<tr>
<td>SN3</td>
<td>Menieres Disease</td>
<td>Left</td>
<td>71</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>18</td>
<td>89</td>
</tr>
</tbody>
</table>

Table 4 | CNC phoneme scores for each subject group at each S/N ratio

<table>
<thead>
<tr>
<th>S/N Ratio</th>
<th>+20 dB</th>
<th>+10 dB</th>
<th>+5 dB</th>
<th>0 dB</th>
<th>Group total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 30)</td>
<td>977 (1.4)</td>
<td>90.3 (3.6)</td>
<td>796 (5.3)</td>
<td>609 (4.8)</td>
<td>82.1 (4.5)</td>
</tr>
<tr>
<td>FRDA without AN/AD (n = 7)</td>
<td>894 (11.2)</td>
<td>75.3 (16.0)</td>
<td>55.3 (13.6)</td>
<td>297 (15.4)</td>
<td>62.4 (26.5)</td>
</tr>
<tr>
<td>FRDA with AN/AD (n = 3)</td>
<td>673 (15.9)</td>
<td>25.9 (3.7)</td>
<td>10.1 (4.0)</td>
<td>0.0 (0.0)</td>
<td>25.8 (277)</td>
</tr>
<tr>
<td>Condition total</td>
<td>94.7 (91)</td>
<td>84.4 (170)</td>
<td>72.1 (191)</td>
<td>53.0 (18.7)</td>
<td></td>
</tr>
</tbody>
</table>

Mean values are shown with standard deviation values in parenthesis.
Post hoc comparison at each SNR revealed that phoneme scores for the normal hearing control group were significantly higher than for the two FRDA groups, and that the FRDA group without AN/AD scored higher than the FRDA with AN/AD group.

**Within-subject noise effects**

Figure 2 shows the CNC phoneme score obtained at each signal to noise ratio for each of the subjects with FRDA. Regression slopes describing the change in CNC-phoneme score with decreasing S/N ratio were established for each of these subjects and for the normal controls. Analysis of variance compared the findings for each of the three subject groups. Overall there was a significant group effect \( F(2,37) = 89.6, P < 0.001 \). Post hoc analysis revealed that the slope of the performance function (i.e. the effect of increasing background noise) was greater in the subjects with FRDA than in those with normal hearing. Furthermore, the subjects with FRDA and AN/AD showed steeper performance decline than those with FRDA without AN/AD. Mean regression values for each subject category are shown in Table 5.

Regression analyses comparing the gradient of the speech perception performance for the 10 FRDA subjects showed no correlation with disease duration \( P = 0.525 \) or GAA1 repeat size \( P = 0.681 \). A significant correlation was, however, found between performance gradient and FARS score with subjects presenting with the greatest overall level of functional disability (highest FARS score) showing more dramatic speech perception performance decline in background noise \( r = 0.634, P = 0.049 \). There was a trend towards greater noise effects in FRDA subjects with earlier disease onset, but the Pearson \( r \) result in this case was not significant \( P = 0.061 \).

**Part 2—Transmission analysis**

Six information transmission analyses were performed on the consonants within the CNC assessment for fricative, sibilant, plosive, burst, semivowel and nasal phoneme groups. The individual phonemes included in each category were as defined by Mok et al. (2006) [Phoneme groupings were as follows: fricatives (/f/, /s/, /θ/, /h/) and sibilants (/ʃ/, /ʒ/); plosives (/b/, /d/, /t/, /g/); bursts (/b/, /d/, /t/, /g/, /k/); semivowels (/l/, /w/, /r/, /j/, /l/); nasals (/m/, /n/, /ŋ/); diphthongs (/æl/, /ær/, /a/, /u/, /ou/)]. The transmission scores for each of these analyses represent the subjects’ ability to classify a speech sound as belonging to a particular phoneme group. Three information transmission analyses were also performed to assess perception of vowel features in the CNC responses.

Transmission analysis results for the FRDA with AN/AD and SN subject groups are shown in Fig. 3. While findings for vowels were broadly equivalent for the two subject groups, the level of information transmission observed across the consonant categories was dissimilar in some cases. A Mann–Whitney analysis revealed that the median information transmission percentage for the AN/AD group was significantly higher than that of the SN group for the ‘sibilant’ phoneme group \( P = 0.008 \). Mann–Whitney comparisons for the other phoneme categories failed to reach significance, although as shown in Fig. 3, there was a trend towards poorer performance in the AN/AD listeners for the ‘semivowel’, ‘nasal’ and ‘diphthong’ groups.

![Fig. 2](https://academic.oup.com/brain/article-abstract/131/8/2002/265873/18202/2012/2007)  
**Fig. 2** CNC-phoneme scores for each of the FRDA subjects plotted as a function of listening condition. Open circles represent the FRDA with AN/AD subjects and filled circles the FRDA without AN/AD subjects. The shaded area shows the performance range (Mean ± 2 SD) for the normal group.

**Table 5** Mean regression slope values describing CNC phoneme/SNR functions for each of the subject groups.

<table>
<thead>
<tr>
<th>Subject group</th>
<th>Performance gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal ((n = 30))</td>
<td>1.74 ± 0.22</td>
</tr>
<tr>
<td>FRDA without AN/AD ((n = 7))</td>
<td>2.75 ± 0.34</td>
</tr>
<tr>
<td>FRDA with AN/AD ((n = 3))</td>
<td>3.61 ± 0.56</td>
</tr>
</tbody>
</table>

![Fig. 3](https://academic.oup.com/brain/article-abstract/131/8/2002/265873/18202/2012/2007)  
**Fig. 3** Information transmission scores for consonant and vowel phoneme categories.
In addition to the aforementioned general analyses that provide an overall picture of phoneme categorization ability, transmission analysis of some specific phoneme pairs was also carried out. Figure 4 shows findings for three stop-consonant pairs. These speech sounds were selected because the phonemes in each pair are similar in all of their articulatory features apart from 'voicing' (A 'voiced' sound is one which is produced with the vocal cords vibrating. The stop consonants /p, t & k/ for example are all unvoiced whereas /b, d & g/ are all voiced). As can be seen in Fig. 4, the subjects with SN hearing loss were better able to differentiate between the voiced and voiceless item in each pair than their AN/AD counterparts. Mann–Whitney analyses showed a significant difference in the percentage of information transmitted for both the /p & b/ (\( P = 0.036 \)) and /t & d/ (\( P = 0.008 \)) contrasts. The difference between subject groups was not significant for the /k & g/ comparison (\( P = 0.320 \)).

Two further transmission analyses involving consonant pairs with phonemes differing in their place of articulation were undertaken (In order to form consonants the airstream through the vocal tract must be obstructed in some way. Where this occurs is referred to as the ‘place of articulation’. For example, /f & v/ are produced by constriction at the front of the mouth where /s & z/ are produced in the same way, but further back in the vocal tract) [Fig. 5]. Mann–Whitney tests again showed significant differences between subject groups (/s & f/, \( P = 0.008 \); /z & v/, \( P = 0.008 \)), but on these comparisons it was the AN/AD subjects who were better able to discriminate the target phonemes.

### Discussion

The audiometric results obtained for the subjects with FRDA in this study were consistent with previous findings that have measured hearing difficulty in terms of sound detection. In studies involving large series’ of individuals with the condition, only 8–13% of patients have demonstrated significantly elevated hearing thresholds although it is not clear how many of these cohort had formal audiology (Harding et al., 1981; Durr et al., 1996). Nine of the 10 subjects in our series showed hearing within normal limits (three-frequency average hearing levels of \( \leq 20 \text{dBHL} \)) and the one subject with significantly elevated hearing levels showed only a mild-degree loss.

However, the ability to detect sound at low levels does not guarantee normal auditory function in individuals with FRDA. Three of the 10 participants in our series showed clear evidence of auditory pathway disorder, presenting with the AN/AD result pattern (abnormal ABR potentials in conjunction with recordable responses from the cochlear hair cells). Interestingly, the degree of auditory neural disruption in these individuals with FRDA reflected the overall disease progression. Results on the FARS (Subramony et al., 2005) indicated that the subjects in this study with the AN/AD result pattern were those who suffered the greatest overall level of functional disability (Table 1).

Open-set speech discrimination was poorer in the subjects with FRDA than in the healthy controls. Even in the quiet listening condition, the FRDA subjects with AN/AD were only able to correctly imitate two out of every three phonemes on the CNC word test. The subjects with FRDA who did not have AN/AD were less affected, with some individuals showing performance levels within the ‘normal’ range, but as a group they still showed an average phoneme score of 89% while the normal controls scored close to 100% in this listening condition. The fact that the subjects with FRDA (particularly those with AN/AD) in this study showed reduced perceptual ability despite enjoying complete access to the speech spectrum, suggests that signal distortion rather than audibility was the limiting factor. Similarly, poor speech perception ability in quiet has been previously reported both in FRDA subjects with AN/AD (Starr et al., 1996; Sininger and Oba, 2001) and in the broader population of subjects with this result pattern (for a review see Rance, 2005).

Cognitive impairment, in particular, deficits in attentional capacities could not be seen as contributing to lower speech recognition scores in people with FRDA. While the
literature on the cognitive components of FRDA is suggestive of reduced information processing speed in the setting of intact executive function, studies examining auditory attention (White et al., 2000; Wollmann et al., 2002) have demonstrated no significant difference in the attentional capacity of people with FRDA compared with control participants.

Auditory perceptual limitations, which in some of the individuals with FRDA were not obvious in quiet, became more pronounced in more challenging listening circumstances. Group CNC phoneme scores obtained in the presence of background noise were again poorest for the AN/AD subjects, but in each of the noise conditions, mean performance levels for both of the FRDA groups were significantly worse than those obtained for the healthy cohort. Furthermore, speech perception performance gradients, which described the reduction in perceptual ability with decreasing SNR for each subject, were steeper for subjects in both FRDA groups than for the normal controls, again demonstrating that the subjects with FRDA were more affected by the competing signal.

The effect of background noise on open-set speech understanding was most clearly demonstrated in the AN/AD subjects who in the +5 dB listening condition scored at near chance levels (correctly imitating only around 10% of phonemes) and at the +0 dB showed no ability to discriminate speech sounds from the background noise at all. This inability to cope with competing signals represents a significant communication challenge as average SNRs in everyday listening environments (offices, school classrooms etc) are typically only around 0–3 dB (Crandell and Smaldino, 2000).

In addition to the aforementioned open-set tests, speech perception ability in noise was also measured using the ADSPON closed-set task. This assessment was included in the battery in part because it requires a ‘pointing’, rather than ‘imitation’ response. While we have no evidence that any of the FRDA subjects involved in the study suffered conditions (such as severe dysarthria) that might have affected their speech intelligibility, it was possible that speech production issues may have impacted slightly upon the CNC phoneme scores (Blaney and Hewlett, 2007). As with the open-set findings, results on the ADSPON test showed clear differences in listening-in-noise ability between groups. Once again, the AN/AD subjects were most affected, requiring the highest SNR (−1.3 dB) before they could reliably identify the test items in noise. This performance level is similar to that obtained previously for a group of school-aged children with AN/AD (Rance et al., 2007) and is >10 dB worse than the result obtained for the healthy controls in this study. That is, the normal subjects demonstrated the same performance level with an extra 10 dB of noise masking the signal. Results for the subjects with FRDA without AN/AD were also poorer than for the normal hearing cohort showing a 4.5 dB greater masking effect (on average) in noise.

Problems with listening in noise have not previously been reported in patients with FRDA, but have been well documented in ears with AN/AD type hearing loss (Starr et al., 1998; Kraus et al., 2000; Shallop, 2002; Ramirez and Mann, 2005). The mechanisms underlying excessive noise effects on speech understanding in this group are, as yet, unclear. However, there is strong psychophysical evidence suggesting that basic auditory signals are more affected by simultaneous masking noise (where the signal and noise are present at the same time) in AN/AD subjects than in normal listeners. A number of studies (Kraus et al., 2000; Zeng et al., 2005; Vinay and Moore, 2007) for example, have shown excessive masking effects (10–20 dB higher than for normal controls) for detection of pure tones in noise. These findings are analogous to the 10 dB masking difference (between AN/AD and normal subjects) obtained for speech stimuli on the ADSPON test in this study.

Psychophysical data has also pointed to temporal processing-related masking effects in AN/AD patients, which may impact upon speech perception ability. Both forward and backward masking experiments (where detection of a brief tone is measured in the proximity of a masking noise) have shown that signals within 100 ms of a masker are difficult for listeners with AN/AD to perceive (Kraus et al., 2000; Zeng et al., 2005). Normal hearing subjects in contrast, show little effect for signals >20 ms from the masker (Zeng et al., 2005). As such, it appears that AN/AD listeners are less able to separate sounds occurring successively. In an everyday listening context, where the level of background noise fluctuates, this temporal processing deficit might impair the listener’s ability to use brief gaps in the noise to optimize speech understanding.

**Disruption of speech cues in subjects with AN/AD**

While degree of temporal disruption has been strongly correlated with overall speech perception ability in subjects with AN/AD (Zeng et al., 1999; Rance et al., 2004) the ways in which this form of processing abnormality affect perception (at the feature level) are yet to be fully considered. Only Kraus et al. (2000) in a single-subject study have shown that an inability to detect brief gaps in the speech signal may affect the perception of subtle vowel features such as third formant onset frequency. Part B of this study used information transmission analyses to determine the pattern of perceptual strengths and weaknesses in the three subjects with FRDA and AN/AD type hearing loss, and in a group of subjects with SN hearing loss who had been matched for overall speech perception ability.

Subjects in both the AN/AD and SN groups were consistently able to categorize the vowels in the CNC-word test on the basis of first and second formant frequency. The ability to make these discriminations are contingent upon the listener’s ‘frequency resolution’. Frequency resolution is the capacity to separate or ‘resolve’ components (in this
case formant energy peaks) in a complex sound. This basic spectral processing occurs at the level of the cochlea and as individuals with AN/AD typically have normal cochlear function, they tend to show normal frequency resolution (Rance et al., 2004; Vinay and Moore, 2007). As such, it is not surprising that the FRDA subjects in this study with AN/AD should discriminate vowel information reasonably well.

Consonant perception in contrast, was greatly impaired in the subjects with AN/AD, and the pattern of discrimination errors was quite different in the two hearing loss groups. The biggest (and only statistically significant) difference between the AN/AD and SN groups was for the ‘sibilant’ phoneme group. Sibilants are a sub-set of the fricative phoneme family, have a high proportion of their acoustic energy in the high frequency range and are characterized by a ‘hissing’ noise (e.g. /s/). Identifying a sound as being a sibilant, therefore, requires accurate high frequency pitch discrimination. As previous studies have shown good high frequency discrimination in individuals with AN/AD (Rance et al., 2004; Zeng et al., 2005) it is not surprising that they should have good information transmission in this category. The subjects with SN in contrast performed relatively poorly for this phoneme categorization. Closer examination of the confusion matrices (the pattern of errors) for these listeners suggested that they tended to mistake the sibilant sound /s/ for the fricative /f/, and the sibilant /z/ for the fricative /v/. These confusions reflect an inability to perceive high frequency spectral differences in the speech sounds and are consistent with previous findings for ears with SN loss (Preminger and Wiley, 1983; Thibodeau and Van Tassell, 1987).

One phoneme category that showed a trend towards poorer performance in the AN/AD subjects involved the perception of nasal consonants. Identification of nasals requires discrimination of low frequency spectral cues. This poor result is consistent with psychophysical evidence suggesting that discrimination in the low spectral range (which relies in part on temporally precise neural firing in the auditory pathway to produce stimulus ‘phase-locking’ cues) is severely disordered in patients with AN/AD (Rance et al., 2004; Zeng et al., 2005).

Information transmission for the semivowel and diphthong categories was also poor for the AN/AD patients. Discrimination in these phoneme groups requires not only accurate low frequency pitch perception, but also the ability to track rapid spectral changes within the speech sounds. Hence, where these subjects could cope well with vowels (which have constant acoustic properties throughout the sound), perception of diphthongs (which are vowel-like but involve changes in formant frequency over the course of the phoneme) was significantly impaired. Again, previous psychophysical work has shown that temporal processing deficits in AN/AD subjects make perception of dynamic signals especially challenging (Rance et al., 2004; Zeng et al., 2005). Furthermore, Quine et al. (1984) found a reduced ability to detect ‘formant transitions’ in computer generated speech-like sounds in four individuals with FRDA.

The ability to use subtle timing cues to discriminate speech sounds was further investigated through specific transmission analyses involving the stop-consonant pairs /p & b/, /t & d/ and /k & g/. The phonemes in these pairs are similar in their articulatory features apart from consonant voicing, and hence, the most salient acoustic difference between the items was the ‘voice onset time’. Voice onset time is the period required for vocal cord vibration to begin after the release of a closure in the vocal tract. In the phoneme pair /p & b/ (where the closure occurs at the lips), voicing resumes 10–30 ms sooner for the voiced sound /b/ than it does for the unvoiced /p/. For the /t & d/ pair there is typically a 20–40 ms difference, and for /k & g/ a 20–45 ms difference (Bennett and Ling, 1973).

The capacity of the subjects with AN/AD to make these discriminations was poor, particularly for the /p & b/ and /t & d/ comparisons, which required the perception of more subtle timing differences. This result is entirely consistent with the psychophysical evidence suggesting an inability to detect brief acoustic cues (Zeng et al., 2005) in individuals with AN/AD. For example, ‘gap-detection’ experiments, which determine the shortest detectable silent period in a burst of noise (essentially the same acoustic challenge as identifying the silent period in stop-consonants) have shown that where listeners with normal hearing can perceive gaps of <5 ms, listeners with AN/AD typically require silent periods of 20 ms or more. The fact that the subjects with SN hearing loss had little difficulty making these discriminations is also consistent with previous findings, which have shown that SN hearing loss does not greatly affect either gap detection, or the perception of timing cues in speech (Turner et al., 1995).

Perception of spectral cues was investigated through transmission analyses of the phoneme pairs /s & f/ and /z & v/. These fricative pairs were selected as they differed only in their place-of-articulation and hence their frequency content. The phonemes /s/ and /z/ for example contain most of their energy at 4 kHz and above, whereas /f/ and /v/ are typically produced with a broad spread of energy from 1 kHz to 8 kHz. As discussed previously, high frequency discrimination tends to be unaffected by AN/AD type hearing loss (as it is not dependent upon temporally precise neural firing), and not surprisingly, the subjects with AN/AD were able to make these frequency-based phoneme discriminations reasonably accurately. In contrast, findings for the SN subjects showed consistent confusion of the target phonemes. This may in part relate to signal audibility, as fricatives are amongst the softest speech sounds, and these subjects all had significant hearing loss. At the speech presentation levels used in this study, however, all of the phonemes should have been audible. Certainly, the finding that these subjects could not reliably make phoneme discriminations based upon spectral cues is expected given
the previous results for ears with SN loss (Preminger et al., 1985; Thibodeau and Van Tasell, 1987).

Another factor that could potentially have influenced the perceptual results in this study was the age of the participants. Where the FRDA subjects with AN/AD were 33–40 years at assessment, the SN subjects were aged 56–67 years. A number of studies have suggested that elderly adults (with and without SN hearing loss) can experience speech understanding difficulties (Jerger et al., 1989; Humes, 1996). These deficits are, however, thought to be primarily related to the processing of temporal rather than spectral cues (Tremblay et al., 2003; Gordon-Salant and Yeni-Komshian, 2006; Shrivastav et al., 2006). As such, any age-related effects in our SN subjects would be expected to make them more like their AN/AD counterparts and yet we still observed clear differences in the pattern of perceptual errors between groups.

**Summary and recommendations**

The auditory evoked potential results in this study indicate that FRDA affects the central auditory brainstem and not the periphery. Furthermore, the findings suggest that it is the number of neural elements that is at issue rather than the speed or efficiency of conduction.

The findings suggest that a relatively high proportion of FRDA patients may suffer hearing difficulties (particularly with speech understanding in background noise) despite in most cases showing normal sound detection levels. Nine of the 10 subjects showed abnormal speech perception scores when tested with levels of noise typical of everyday listening conditions. As such, regular auditory assessment should be part of the management regime for all individuals with FRDA, and should involve auditory evoked potential and auditory processing (speech perception in noise) testing.

Management of individuals with inherent auditory processing limitations is problematic. There is currently no evidence that training is beneficial, and the provision of conventional hearing aids (which are designed to make sounds louder rather than improve signal clarity) tend not to be useful (Starr et al., 1996). Speech processing devices, which can manipulate the speech signal to address the specific perceptual deficits highlighted by this study, may however, be an option for the future (Zeng et al., 2001).

Finally, provision of communication training including the use of listening tactics, lip-reading cues etc. may be helpful in maximizing non-auditory information transmission as will fostering an awareness of the importance of optimal (quiet) listening conditions. The use of radio-frequency listening devices (where the speaker is fit with a transmitter and the listener wears a receiver) may also be useful for improving SNR in some circumstances. This can be particularly helpful in settings where difficulties are regularly and predictably encountered such as the office or classroom (Anderson and Goldstein, 2004).

**Acknowledgements**

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**References**


