The Journal of Laryngology & Otology (2010), ***124***, *950–956.*

doi:10.1017/S0022215110000630

Main Article

Auditory steady state response in auditory neuropathy

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Abstract

Review: Auditory neuropathy is a disorder characterised by preservation of outer hair cell function, with normal otoacoustic emissions and/or cochlear microphonics, but an absent or distorted auditory brainstem response.

Purpose: This study aimed to objectively assess hearing thresholds in patients with auditory neuropathy, using the auditory steady state response.

Materials and methods: Thirteen patients with auditory neuropathy and 15 normal hearing subjects were examined. Audiological evaluation included basic audiological tests, otoacoustic emissions, auditory brainstem response and auditory steady state response.

Results: In the auditory neuropathy patients, the auditory brainstem response was absent in 11 patients, while the auditory steady state response was absent in only three.

Conclusion: The auditory steady state response may serve as a valuable objective measure for assessing the hearing threshold across different frequencies in patients with auditory neuropathy. We recommend that auditory steady state response be used to complete the evaluation of patients with auditory neuropathy.

Key words: Auditory Neuropathy; Cochlea; Auditory Brainstem Response; Audiometry; Otoacoustic Emissions; Psychoacoustics

Introduction

Auditory neuropathy is a term used to describe a range of disorders found in paediatric and adult patients. Clinically, patients with auditory neuropathy have normal otoacoustic emissions (OAEs) and/or cochlear microphonics but absent or severely abnormal auditory brainstem responses (ABRs). Over the years, many cases of auditory neuropathy have been reported, with a wide spectrum of symptoms. However, most reported cases share some common characteristics. Individuals with auditory neuropathy have pure tone thresholds that vary from normal to profound hearing loss, with a variety of audiometric configurations. The majority of patients have mild to moderate hearing loss, and have difficulty understanding speech in at least some situations.[1,2]

Several pathological mechanisms have been suggested to be involved in the development of auditory neuropathy. These include auditory synaptic deficiency and auditory nerve myelinopathy and/or desynchrony of neural discharges; however, the exact site of pathology remains undetermined.[3]

Auditory neuropathy occurs much more frequently than initially anticipated. It represents as much as 8 per cent of newly diagnosed cases of paediatric hearing loss per year.[4] Auditory neuropathy is categorised according to the age of onset, into two distinct groups: an early onset form, typically associated with a neonatal insult; and a delayed onset form, usually accompanied by generalised neuropathy. However, only 25 per cent of auditory neuropathy patients are older than 10 years when symptoms initially occur.[5]

The ABR can be used as an objective tool for estimating the hearing threshold. However, it is usually absent, or severely distorted and disproportionate to hearing threshold levels, in auditory neuropathy patients.[6] This occurs because ABR recording is highly dependent on neural synchrony, which is compromised in auditory neuropathy patients regardless of their degree of hearing loss or the level of test stimulus.[7]

Measurement of the auditory steady state response is an accurate method for estimating the hearing threshold.[8] This response is an evoked potential the constituent frequency components of which remain constant in amplitude and phase over time. Auditory steady state response is generally measured in the frequency domain. Therefore, only those peaks in the spectrum of the stimulus or its harmonics are considered.[9]

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Presented at the 6th Tanta International Conference on Advanced Otorhinolaryngology, 15–16 January 2009, Scientific Sessions (Cairo Sheraton Hotel), Tanta, Egypt.
Accepted for publication: 6 January 2010. First published online 14 April 2010.

Aims

This study was designed to investigate the use of the auditory steady state response as an objective assessment of hearing thresholds in patients with auditory neuropathy whose ABR (to clicks) was absent or significantly impaired. The study was also designed to assess the correlation between behavioural and auditory steady state response thresholds, in these patients.

Materials and methods

This study included two groups.

Group one (the study group) consisted of 13 patients with auditory neuropathy (five men and eight women), aged between 16 and 41 years.

Group II (the control group) consisted of 15 normal hearing subjects whose age and gender were matched to those of the auditory neuropathy patients. All these subjects had bilateral normal peripheral and middle-ear function.

The study was conducted in the audiology unit of the ENT department, Tanta University Hospital, between April and December 2008. Verbal consent was obtained from all study participants.

Subjects included in the study underwent full audiological history-taking, otological examination and basic audiological evaluation (including pure tone audiometry (250–8000 Hz), speech audiometry and immittancemetry). All auditory neuropathy patients underwent otoacoustic emissions testing (either transient evoked OAEs (TEOAs) or distortion product OAEs (DPOAEs), according to patients' hearing thresholds).

Auditory brainstem response

Ipsilateral click stimuli were presented at 90 dBHL, with alternating polarity, with a 19.3/second repetition rate, delivered via an ER3A insertphone of SmartEPs (TM, Intelligent Hearing system, Miami, USA). When the ABR was recorded at this intensity level, it was traced down to the hearing threshold. Three electrodes were used: a positive electrode high on the forehead, a negative electrode on the ipsilateral mastoid and a ground electrode at the contralateral mastoid.

Auditory steady state response

This was evoked by a binaural multifrequency paradigm, using the Smart-EPs Intelligent Hearing System (TM, Intelligent Hearing system, Miami, USA). This paradigm involves the simultaneous presentation of stimuli to both ears at the same carrier frequency but at different modulation rates. The carrier frequencies were 500, 1000, 2000 and 4000 Hz. The modulation rates were 77, 85, 93 and 101 Hz in the right ear, and 79, 87, 95 and 103 Hz in the left ear, for carrier frequencies of 500 to 4000 Hz, i.e. 500, 1000, 2000 and 4000 Hz, respectively. Test stimuli were presented via ER3A insertphones calibrated in dBSPL. The stimulation intensity was presented starting at 90 dBSPL. All subjects were tested in a relaxed state, on a comfortable bed in a quiet room.

Four electrodes were used: a positive electrode high on the forehead, a ground electrode lower on the forehead and two negative electrodes placed at both mastoids. Fast Fourier transforms were used to elicit the auditory steady state response. Only responses with a high signal-to-noise ratio were accepted by the equipment. When a significant response was obtained at the starting level, the intensity was lowered by 10 dB steps to obtain thresholds in both ears. The auditory steady state response threshold was defined as the lowest intensity at which there was a significant response. Monaural stimulation and single frequency testing were performed when there was no response to binaural stimulation.[10] The auditory steady state response was considered absent if there was no response at the maximum number of sweeps of the equipment (400 sweeps). Auditory steady state response was recorded in dBSPL and then converted into dBHL.

Statistical analysis

The paired Student *t*-test was used to compare the pure tone average (PTA) threshold and the auditory steady state response threshold. The Pearson test was used to assess the correlation between the two thresholds.

Results

Twenty-eight subjects were included in the study.

Group one comprised 13 auditory neuropathy patients (five men and eight women; mean age ± standard deviation (SD) 22.6 ± 5.9 years). Their duration of hearing loss ranged from six months to 10 years. Patients' hearing loss configuration was low frequency in 10 patients (76.92 per cent), high frequency in one patient (7.69 per cent) and flat in two patients (15.38 per cent) (Table I). Patients' mean ± SD PTA threshold levels were 47.5 ± 20.45, 44.72 ± 15.76, 35.0 ± 16.27 and 30.83 ± 19.35 dB for 500,

TABLE I

AUDITORY NEUROPATHY PATIENTS: GENDER AND AUDIOLOGICAL RESULTS

Parameter	Pts	
	n	%
Gender		
F	8	61.54
M	5	38.46
PTA pattern		
HF	1	7.69
LF	10	76.92
Flat	2	15.38
ABR		
Absent	11	84.62
Present	2	15.38
ASSR		
Absent	3	23.1
Present	10	76.9

F = female; M = male; PTA = pure tone average; HF = high frequency; LF = low frequency; ABR = auditory brainstem response; ASSR = auditory steady state response

https://doi.org/10.1017/S0022215110000630 Published online by Cambridge University Press

TABLE II

AUDITORY NEUROPATHY PATIENTS: INDIVIDUAL DATA

Pt no	Aetiology	Hearing loss			ABR	ASSR
		Side	Severity	Pattern		
1	–	Bilat	Mod	LF	Absent	Present
2	–	Bilat	Mod	Flat	Absent	Present
3	–	Bilat	Mod	LF	Absent	Absent
4	–	Bilat	Mild	LF	Absent	Absent
5	Fever	Unilat	Mild	LF	Present	Present
6	Jaundice	Bilat	Mild	LF	Present	Present
7	Fever	Bilat	Mod	LF	Absent	Present
8	Fever	Bilat	Mild	LF	Absent	Present
9	–	Bilat	Mild	LF	Absent	Present
10	–	Bilat	Mod	HF	Absent	Absent
11	Jaundice	Bilat	Mild	Flat	Absent	Present
12	Jaundice	Bilat	Mild	LF	Absent	Present
13	Jaundice	Bilat	Mild	LF	Absent	Present

Pt no = patient number; ABR = auditory brainstem response; ASSR = auditory steady state response; – = unknown aetiology; bilat = bilateral; unilat = unilateral; mod = moderate; LF = low frequency; HF = high frequency

TABLE III

PURE TONE AVERAGE *VS* AUDITORY STEADY STATE RESPONSE THRESHOLDS: AUDITORY NEUROPATHY PATIENTS

Parameter	Frequency (Hz)			
	500	1000	2000	4000
PTA	47.5 ± 20.45	44.72 ± 15.76	35.0 ± 16.27	30.83 ± 19.35
ASSR	60.62 ± 25.35	64.44 ± 20.57	58.23 ± 32.06	54.0 ± 27.3
t-test	1.669	3.229	2.727	2.727
p	0.105	0.003*	0.010*	0.008*
Mean diff	13.12	19.72	23.23	23.17
CI	13.12 ± 9.4	19.72 ± 7.48	23.23 ± 10.37	23.17 ± 9.65

*$p < 0.05$. PTA = pure tone average; ASSR = auditory steady state response; diff = difference; CI = confidence interval of the difference

1000, 2000 and 4000 Hz, respectively. An auditory steady state response was present in 10 patients (76.9 per cent) and absent in three (23.07 per cent) (Table I). Table II shows patients' aetiology, degree, configuration and laterality of hearing loss.

In group one patients, the mean ± SD auditory steady state response thresholds were 60.62 ± 25.35, 64.44 ± 20.57, 58.23 ± 32.06 and 54.0 ± 27.3 dBHL for 500, 1000, 2000 and 4000 Hz, respectively.

Comparison between the group one patients' PTA thresholds and auditory steady state response thresholds revealed a statistically significant difference at 1000, 2000 and 4000 Hz carrier frequencies ($p < 0.05$). There was no statistically significant difference at 500 Hz ($p > 0.05$). The differences between the PTA and auditory steady state response thresholds in the group one patients were 13.12, 19.72, 23.23 and 23.8 dBHL at 500, 1000, 2000 and 4000 Hz, respectively (Table III and Figures 1 and 2).

Group two (the control group) comprised 15 normal hearing subjects (seven men and eight women; mean age ± SD 26.4 ± 5.2 years; there was no statistically significant age difference between the two groups). These subjects' mean ± SD PTA threshold levels were 12.0 ± 4.93, 8.0 ± 3.68, 6.0 ± 3.38 and 5.33 ± 3.52 dBHL for 500, 1000, 2000 and 4000 Hz, respectively. Their auditory steady state response thresholds were 29.33 ± 9.8, 24.67 ± 5.81, 23.0 ± 9.41 and 14.33 ± 9.8 dBHL for 500, 1000, 2000 and 4000 Hz, respectively.

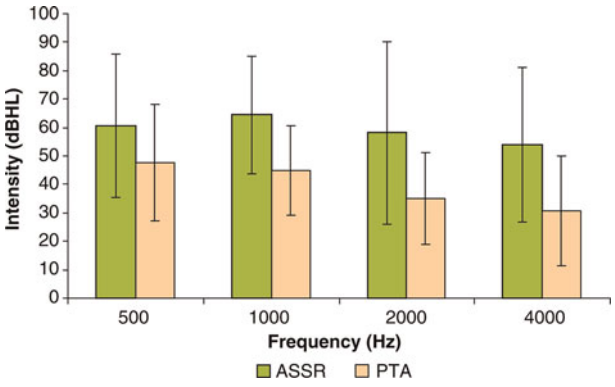

FIG. 1

Mean and standard deviation (whiskers) of auditory steady state response (ASSR) and pure tone average (PTA) thresholds at test frequencies, in auditory neuropathy patients.

When the group two subjects' PTA and auditory steady state response thresholds were compared, there was a statistically significant difference at all frequencies ($p < 0.05$). The differences between PTA and auditory steady state response thresholds were 17.33, 16.67, 17.0 and 9.0 dBHL at 500, 1000, 2000, and 4000 Hz, respectively (Table IV and Figures 3 and 4).

The Pearson test was performed to assess the correlation between the PTA and auditory steady state response thresholds, at each carrier frequency, in both groups. No correlation between the two

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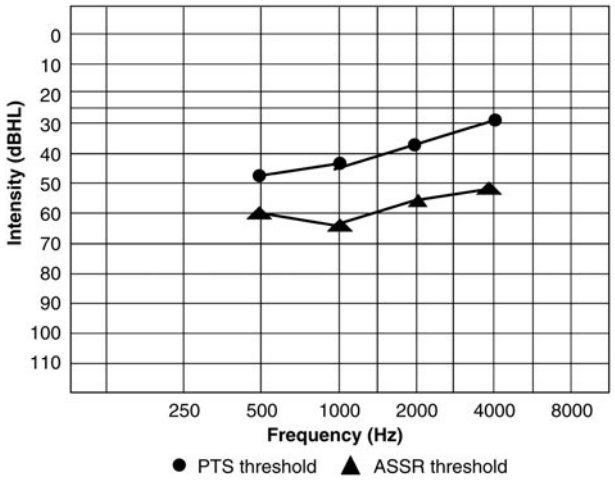

FIG. 2

Mean pure tone average (PTA) and auditory steady state response (ASSR) thresholds at test frequencies, in auditory neuropathy patients.

thresholds was found in group one (Table V). However, there was a strong correlation between the two thresholds in group two (Table VI).

In group one, TE OAEs and DPOAEs were present in all patients, while ABRs were present in two patients (15.38 per cent) and absent in 11 (84.62 per cent) (Table I).

Discussion

Auditory neuropathy, or auditory dys-synchrony, is defined by an abnormal or absent auditory brainstem response in the presence of intact otoacoustic emissions and/or cochlear microphonics. It is associated with impaired hearing results on behavioural pure tone audiometry, absent acoustic reflexes, and poor speech perception particularly in noisy environments. These results suggest a disorder of inner hair cell and/or VIIIth nerve function. This is a condition in which the cochlea appears to function normally but there is a problem with the nerves, so that sound cannot be normally processed and the ABR is missing or abnormal. A patient with auditory neuropathy may appear to hear one day and not hear the next.[11]

Our auditory neuropathy patients' auditory steady state response thresholds were significantly higher than their PTA thresholds, except at 500Hz. This result agrees with the findings of Attias *et al.*[10] At the same time, the two thresholds did not correlate at any frequency. This is consistent with the results of Rance *et al.*, and Toca and Savio Lope.[12,13]

Our normal hearing subjects' auditory steady state response thresholds were also higher than their PTA thresholds, and this was statistically significant at all frequencies. There was a correlation between PTA and auditory steady state response thresholds. This was consistent with Attias and colleagues' results.[10]

In the current study, an ABR was recorded in only two of the 13 patients with auditory neuropathy (15.4 per cent), which was disproportionate to PTA thresholds. These results are consistent with the poor neural synchronisation found in auditory neuropathy, and agree with the findings of many other authors.[1,14,15] The extraction of the ABR signal from the electroencephalography signal requires precise synchronisation of neural firing. Even minor variations in the timing of neural discharges after each stimulus (e.g. <0.5 msec) can make the ABR response unrecognisable.[12]

Recent information supports the hypothesis that auditory neuropathy is not a single disease but a spectrum of pathologies affecting the auditory pathways.[16] The disease shows some variation on electrophysiological testing. Approximately 20 per cent of auditory neuropathy patients may have a low amplitude wave V in their ABR, indicating that neural synchrony can be partially preserved in some patients with this disorder.[17]

Auditory brainstem responses to click stimuli lack frequency specificity and provide information on only a narrow frequency range (2–4 kHz). At the same time, the use of tone burst ABR prolongs the test duration and is restricted at the transducer output, resulting in ABR absence in patients with severe to profound hearing loss. Moreover, the dependence of ABR on neural synchrony compromises its use in auditory neuropathy patients.[10]

In the current study, the auditory steady state response was recorded in ten of the 13 patients with auditory neuropathy. Thus, auditory steady state responses were detected in many more auditory neuropathy patients, compared with ABR responses. This supports the concept that auditory steady state response, recorded in the frequency domain, is preferable to ABR when examining this group of patients. These findings agree with those of Attias *et al.*[10]

TABLE IV

PURE TONE AVERAGE *VS* AUDITORY STEADY STATE RESPONSE THRESHOLDS: NORMAL HEARING SUBJECTS

Parameter	Frequency (Hz)			
	500	1000	2000	4000
PTA	12 ± 4.93	8 ± 3.68	6 ± 3.38	5.33 ± 3.52
ASSR	29.33 ± 9.8	24.67 ± 5.81	23 ± 9.41	14.33 ± 9.8
t-test	−6.122	−9.38	−6.59	−3.35
p	0.000*	0.000*	0.000*	0.002*
Mean diff	17.33	16.67	17.0	9.0
CI	17.33 ± 14.98	16.67 ± 1.78	17 ± 2.58	9 ± 2.69

*$p < 0.05$. PTA = pure tone average; ASSR = auditory steady state response; diff = difference; CI = confidence interval of the difference

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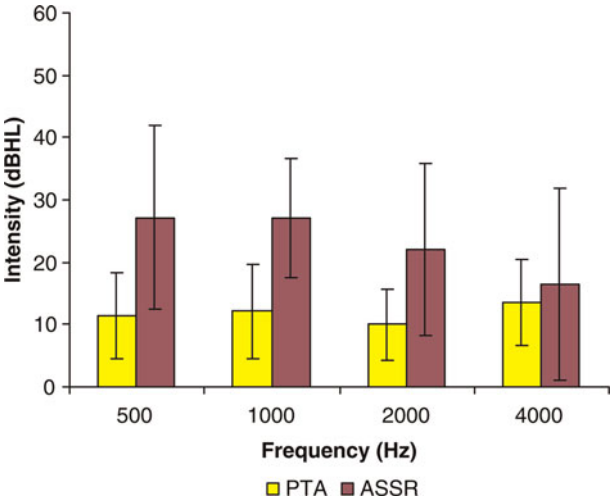

FIG. 3

Mean and standard deviation (whiskers) of auditory steady state response (ASSR) and pure tone average (PTA) thresholds at test frequencies, in normal hearing subjects.

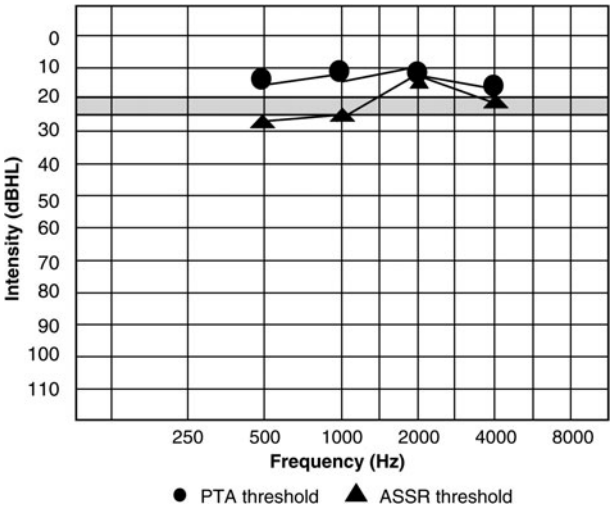

FIG. 4

Mean pure tone average (PTA) and auditory steady state response (ASSR) thresholds at test frequencies, in normal hearing subjects.

In addition, the auditory steady state response is less affected by the neural desynchronisation present in patients with auditory neuropathy. Therefore, it could be used in predicting behavioural hearing thresholds in patients whose threshold is difficult to be obtained or unreliable and ABR results can not be accounted on for such prediction.[18]

The auditory steady state response can serve as an alternative, objective measure combining both frequency specificity and a higher level of stimulation.[19] The tone stimulus used to elicit the auditory steady state response is continuous. Thus, the auditory steady state response does not suffer from the spectral distortion problems associated with tone bursts or clicks.[12] Moreover, the modulated tones used to elicit the auditory steady state response are similar to the warble tones used in behavioural assessment. The calibration corrections required for tone bursts or clicks are therefore not needed, and stimuli can be presented up to 120 dBHL. Recent clinical studies have reported a close correlation between behavioural auditory responses and auditory steady state response thresholds in infants, children and adults. The auditory steady state response could be reliably recorded even in patients with severe SNHL, in whom an ABR to clicks could not be obtained.[20]

The auditory steady state response does not significantly correlate with PTA thresholds in patients with auditory neuropathy; however, it can be applied in those patients to help distinguish different degrees of hearing loss. Similar findings have been reported by Toca and Savio Lope, who demonstrated the usefulness of the auditory steady state response as an objective tool in patients with auditory neuropathy, of similar utility to ABR.[13]

The results of the present study show that the auditory steady state response is affected in auditory neuropathy, although not as much as ABR. This agrees with the findings of Attias *et al.*, who reported that the use of higher stimulus levels during auditory steady state response testing probably increases neural tract synchronisation, resulting in more pronounced responses.[10] These findings seem to support the notion that poor synchronisation is the cause of poor neural responses. Therefore, measuring auditory steady state responses may give more information about frequency-specific hearing thresholds in auditory neuropathy patients, thus increasing the usefulness of this test.

In the current study, auditory steady state responses had good predictive value for behavioural hearing thresholds in subjects with normal hearing, however,

TABLE V

CORRELATION BETWEEN AUDITORY STEADY STATE RESPONSE AND PTA THRESHOLDS AT DIFFERENT FREQUENCIES: AUDITORY NEUROPATHY PATIENTS

PTA	ASSR							
	500 Hz		1000 Hz		2000 Hz		4000 Hz	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
500 Hz	−0.529	0.222						
1000 Hz			0.563	0.188				
2000 Hz					0.732	0.061		
4000 Hz							−0.446	0.316

PTA = pure tone average; ASSR = auditory steady state response

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TABLE VI

CORRELATION BETWEEN AUDITORY STEADY STATE RESPONSE AND PTA THRESHOLDS AT DIFFERENT FREQUENCIES: NORMAL HEARING SUBJECTS

PTA	ASSR							
	500 Hz		1000 Hz		2000 Hz		4000 Hz	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
500 Hz	0.954	0.000						
1000 Hz			0.791	0.000				
2000 Hz					0.909	0.000		
4000 Hz							0.888	0.000

PTA = pure tone average; ASSR = auditory steady state response

they did not correlate with behavioural hearing thresholds in auditory neuropathy patients.[21]

- **The term auditory neuropathy describes a range of disorders found in paediatric and adult patients**
- **These patients have normal otoacoustic emissions and/or cochlear microphonics, but absent or severely abnormal auditory brainstem responses**
- **Auditory neuropathy is associated with impaired hearing on behavioural pure tone audiometry, absent acoustic reflexes, and poor speech perception particularly in noisy environments**
- **This study assessed the use of auditory steady state response testing in such patients**
- **The auditory steady state response has good predictive value for behavioural hearing thresholds in normal hearing subjects; however, it does not correlate with such thresholds in auditory neuropathy patients**

Conclusion

These results support previous findings indicating that hearing threshold levels are not consistent with ABR thresholds in auditory neuropathy patients. However, the absence of an ABR does not preclude the presence of residual hearing. Although auditory steady state responses were found in a larger percentage of auditory neuropathy patients, compared with ABR, the results should be interpreted with caution, especially when this response is absent. We recommend auditory steady state response testing, alongside ABR and OAE measurement, to facilitate better diagnosis of auditory neuropathy.

Further study on a large number of auditory neuropathy patients should be undertaken.

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Dr A A Emara takes responsibility for the integrity of the content of the paper.
Competing interests: None declared