PET $\geq 1{,}000\ mm\ yr^{-1}$. Other factors may predict mammal species richness in tropical regions where mammal distributions are relatively poorly known. As potential evapotranspiration in the American southwest is comparable to that of the Amazonian basin[18], we have sampled almost the entire range of global variation and found that energy is important only in comparatively cold regions.

The nonlinear relationships between diversity and energy availability that we have described may have significant implications for the impacts of climate change on mammal communities. As energy availability increases because of global warming, habitat heterogeneity may become the prime determinant of species richness patterns over an increasing proportion of the North American continent. □

Methods

Description of data. We investigated predictors of mammal species richness in North America using data from ref. 6. We determined the approximate PET contour beyond which PET is unrelated to mammal richness by visual inspection of the PET-richness plot (Fig. 1) and general agreement between the Quasi-Newton, Simplex and Hooke–Jeeves breakpoint estimation routines[19]. The high energy region consists of 130 2.5° × 2.5° quadrats. Independent variables describing mean conditions were determined by averaging maximum and minimum values for the different environmental variables in each quadrat. Those measuring spatial variability were determined by taking the difference between the maximum and minimum values per quadrat for the respective environmental descriptors. Annual temperature variability is the difference between the mean January and July temperatures, respectively, of each quadrat. Glaciation effects were measured by creating a dummy variable describing whether quadrats were clear, inundated or glaciated during the Wisconsinan. Coastal and peninsular location are also dummy variables. Coastal location, in particular, accounts for low richness outliers in our first and third figures.

Statistical analysis. We analysed bivariate plots of species richness and the various predictor variables (Table 1) in this region and tested the observed relations using both forward and backward stepwise regression analysis[19,20]. Quadrat area does not enter our final model. Using correspondingly numbered variables in Table 1, we investigated the following hypotheses of species diversity: (1) species richness–energy[21–23]; (2) climatic favourability[3]; (3) habitat heterogeneity[15]; (4) climatic stability[24]; and (5) glacial history[11]. Variation in both elevation and PET are consistently the most important predictors of mammal richness, regardless of the regression approach used. Additional variables may be added to the regression equation, but contribute little to the predictive power of the model.

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Correspondence and requests for materials should be addressed to J.T.K. (e-mail: jtkerr@yorku. ca).

Impaired auditory recognition of fear and anger following bilateral amygdala lesions

Sophie K. Scott*, Andrew W. Young*, Andrew J. Calder*, Deborah J. Hellawell†, John P. Aggleton‡ & Michael Johnson§

* *MRC Applied Psychology Unit, 15 Chaucer Road, Cambridge CB2 2EF, UK*
† *Rehabilitation Studies Unit, Astley Ainslie Hospital, Grange Loan, Edinburgh EH9 2HL, UK*
‡ *School of Psychology, University of Wales at Cardiff, PO Box 901, Cardiff CF1 3YG, UK*
§ *Department of Neurology, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK*

The amygdalar complex is a medial temporal lobe structure in the brain which is widely considered to be involved in the neural substrates of emotion. Selective bilateral damage to the human amygdala is rare, offering a unique insight into its functions. There is impairment of social perception after amygdala damage, with defective recognition of facial expressions of emotion[1–4]. Among the basic emotions, the processing of fear and anger has been shown to be disrupted by amygdala damage[1,2,5]. Although it remains puzzling why this not found in all cases[6], the importance of the amygdala in negative emotion, and especially fear, has been confirmed by conditioning[7], memory[8] and positron emission tomography (PET) experiments[9,10]. Central to our understanding of these findings is the question of whether the amygdala is involved specifically in the perception of visual signals of emotion emanating from the face, or more widely in the perception of emotion in all sensory modalities[11]. We report here a further investigation of one of these rare cases, a woman (D.R.) who has impaired perception of the intonation patterns that are essential to the perception of vocal affect, despite normal hearing. As is the case for recognition of facial expressions, it is recognition of fear and anger that is most severely affected in the auditory domain. This shows that the amygdala's role in the recognition of certain emotions is not confined to vision, which is consistent with its being involved in the appraisal of danger and the emotion of fear[12,13].

D.R., a woman in her early fifties, first suffered from epilepsy at the age of 28. After anticonvulsant drugs failed to control this, she underwent a series of stereotaxic operations targeted at the left and right amygdala. Tracings of the lesions in the region of the amygdala from magnetic resonance imaging (MRI) scans are shown in Fig. 1.

Following surgery, D.R. could recognize the faces of people who were familiar to her before the operation, and she performed well on unfamiliar face-matching tasks in which the faces had neutral expressions. Hence, there was no general impairment of face perception. In contrast, D.R. showed poor processing of social signals from the face; her judgment of direction of gaze and her interpretation of facial expressions of emotion were impaired[3,4]. For facial expressions, recognition of fear was differentially severely affected, but there was also evidence of impaired recognition of anger and (to a lesser extent) disgust[5].

For the present study, we assessed D.R.'s perception of sounds and voices. Audiometric testing was unremarkable, with hearing within normal limits for her age for all frequencies tested (250–8,000 Hz). Tests from the PALPA battery[14] were used to examine D.R.'s auditory processing of language: the results are shown in Table 1. D.R. had no significant problems in discriminating minimally different pairs of

Table 1 Performance of D.R. on auditory and voice perception tasks

	D.R.	Controls	
		Mean	s.d.
PALPA auditory processing tests			
Discrimination of non-word minimal pairs			
Same	36/36	35.70	0.56
Different	32/36	35.09	2.34
Discrimination of word minimal pairs			
Same	35/36	35.54	0.78
Different	35/36	34.83	2.58
Phonological segmentation of initial sounds			
Words	29/30	29.36	0.86
Non-words	13/15	14.24	1.01
Recognition of environmental sounds			
	15/20	16.85	1.42
Vocal expressions			
Sentence content control task	21/24	23.15	1.35
Tone of voice	17/24**	21.50	1.70
Sentence prosody	9/24***	19.90	3.40
Unfamiliar voice matching			
	27/40***	36.75	2.61
Recognition of familiar voices			
Famous voices			
Recognized as familiar	6/30**	20.30	5.65
Correctly identified	2/30**	15.70	5.88
Unfamiliar voices			
Correct rejections	8/10	9.20	0.77

Control data for the PALPA subtests are taken from the test's norms[14]; from the other tests, control data come from ref. 15. Asterisked scores are significantly below the control mean: * $z > 1.65$, $P < 0.05$; ** $z > 2.33$, $P < 0.01$; *** $z > 3.10$, $P < 0.001$.

spoken nonwords (such as 'zog-zog' vs. 'zog-zeg') or words (such as 'house-house' vs. 'house-mouse'), and she was able to identify the initial phonemes from monosyllabic words and non-words.

We also tested D.R.'s ability to identify environmental sounds, to interpret vocal expressions of emotion, to match unfamiliar voices, and to recognize familiar people from their voices. Full details of these tasks are given elsewhere[15]; D.R.'s performance is summarized in Table 1.

To test recognition of environmental sounds, we used 20 clips of everyday sounds (such as rain or the telephone) lasting 8 s each. D.R. was asked to identify each sound. Her performance fell in the low–normal range (15/20 correct; $z = 1.30$, $P > 0.05$).

For our present purposes, the tasks summarized so far show that any problems that D.R. had in recognizing auditory emotion could not be due to generalized hearing defect. In addition, we established that she understood the meaning of 'emotion' words: D.R. could readily describe circumstances in which other people would experience emotions of happiness, sadness, anger, and so on. To test this formally, a control task was given, in which D.R. was asked whether the content of 24 sentences was happy, angry or sad. She again performed in the low–normal range (21/24 correct; $z = 1.59$, $P > 0.05$), showing adequate comprehension of the meanings of emotional terms.

To assess D.R.'s ability to understand vocal expressions of emotion, she was asked to listen to a tape of 24 sentences with neutral content. These sentences were read with an emotional tone of voice, and D.R. was asked whether each sentence was read in a happy, angry or sad manner. Her performance at identifying emotion from the tone of voice was well below that of the controls (17/24 correct; $z = 2.65$; $P < 0.01$).

Our unfamiliar voice-matching task involved listening to a taped set of 40 trials, on each of which the same sentence was read out twice. For half of these trials, the sentence was read by different people, and for the other half it was read by the same person. D.R.'s performance was very poor (27/40 correct overall; $z = 3.74$, $P < 0.001$) in deciding whether each sentence had been read by the same or different people. A further sentence prosody task involved 24 sentences with neutral content, read with intonation patterns indicating a question, a statement or an exclamation: D.R. was severely impaired at deciding what each sentence was (9/24 correct; $z = 3.21$; $P < 0.001$), performing at chance level (chance = 8/24 correct).

Recognition of familiar voices was tested using 30 famous people's voices and 10 unfamiliar voices, recorded in clips of about 5 s long. D.R. was asked whether each voice was familiar, and if so to identify the person by occupation or name. She performed poorly both at recognizing voices as familiar (6/30 correct; $z = 2.53$, $P < 0.01$) and identifying them (2/30 correct; $z = 2.33$, $P < 0.01$).

Across these tasks, then, D.R. had impaired ability to make use of intonation patterns with communicative significance, including those used in signalling emotion[16]. It is likely that D.R.'s problems in matching unfamiliar voices and recognizing familiar voices also derived from the same source, because intonation patterns form an important determinant of what voices sound like[17,18].

To explore further D.R.'s problems in auditory recognition of emotion, we developed two tasks with enough trials to allow assessment of different basic emotions; data are summarized in Table 2.

The first test involved single words with neutral meanings (for example, carpet), spoken with intonations intended to convey emotions of happiness, sadness, anger, fear or disgust. These emotions were chosen because they are each known to be associated with distinct sets of prosodic features[19]. D.R. showed significantly impaired recognition of anger (3/10 correct; $z = 4.56$; $P < 0.001$) and fear (1/10 correct; $z = 1.93$; $P < 0.05$), and borderline impairments of sadness (6/10 correct; $z = 1.66$; $P = 0.049$) and happiness ($z = 1.62$; $P = 0.053$). Note that the extent of the fear-recognition deficit may be underestimated in this test, owing to the fact that D.R. performed at floor level.

The second test assessed recognition of basic emotions conveyed by entirely non-verbal sound patterns (laughing for happiness, growling for anger, and so on). D.R. showed highly significantly impaired recognition of anger ($z = 3.73$, $P < 0.001$) and fear ($z = 6.89$, $P < 0.001$), and normal performance ($z < 1$, $P > 0.1$) for the other emotions.

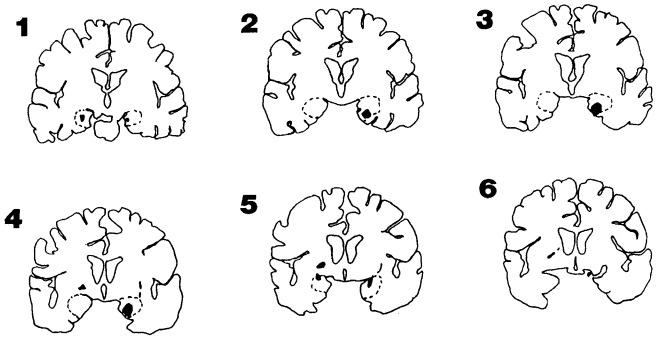

Figure 1 Tracings of lesions in the region of D.R.'s amygdala derived from 6 coronal MRI sections at 2.2-mm intervals. The region of the amygdala is marked by dashed lines, and the regions of damage are indicated in black. The sections are numbered in a caudal to rostral direction, with the left amygdala on the right side of each.

Table 2 Performance of D.R. on auditory emotion recognition tasks

	D.R.	Controls	
		Mean	s.d.
Words			
Happiness	4/10	7.60	2.32
Sadness	6/10*	8.50	1.51
Anger	3/10***	8.20	1.14
Fear	1/10*	4.90	2.02
Disgust	6/10	5.90	1.97
Sounds			
Happiness	15/20	16.33	1.56
Sadness	15/20	16.00	2.00
Anger	5/20***	14.33	2.50
Fear	6/20***	16.33	1.50
Disgust	20/20	18.25	2.22
Surprise	18/20	17.58	1.88

Means and standard deviations are values for control subjects of comparable age and education. Asterisked scores are significantly below the control mean: $*z > 1.65, P < 0.05$; $**z > 2.33, P < 0.01$; $***z > 3.10, P < 0.001$.

Taken together, our findings show that D.R. had impaired interpretation of paralinguistic signals involved in the communication of emotion, despite her normal hearing and speech perception. It is clear that these deficits are not entirely restricted to the recognition of emotion: D.R. had problems in using prosodic features to determine whether a sentence was intended as a question or an exclamation, and even to recognize or match a speaker's identity. When the deficit in recognizing emotion was investigated in more detail, however, it was the recognition of fear and anger that were consistently the most severely impaired. Note particularly that different cues are involved in signalling fear or anger by prosody or non-verbal sounds (screams and growls, for example), so D.R.'s consistent problems with these emotions cannot be reduced to some subtle hearing defect.

The pattern forms a close parallel to previous findings in the visual domain. For D.R., her interpretation is defective of social signals other than emotion from the face, including eye gaze direction[3]. Findings of impaired processing of social signals from face and voice confirm the suggestion that the amygdala forms part of the neural substrate for social cognition[11]. In addition, the recognition of facial expressions of fear and anger is particularly severely compromised for D.R., and there is evidence that the same emotions are affected in the postencephalitic case S.E., who also has bilateral amygdala damage[5]. Although reports of case S.M., who has bilateral amygdala damage due to Urbach–Wiethe disease, emphasize her poor recognition of fear from the face, she is also significantly impaired at recognizing anger in some tests[1,2]. Therefore, recognition of fear and anger in particular seems to be compromised by bilateral amygdala damage, regardless of the input modality.

The fact that D.R.'s recognition of emotion is impaired across the same basic emotions of fear and anger for voices and faces is consistent with impairment of a mechanism geared to interpreting emotional signals regardless of their source, rather than a mechanism specific to faces *per se*. Although it contains many cells responsive to faces seen[20–23], the amygdala is known to receive inputs from other sense modalities[24] and is therefore in a position to be involved in multimodal recognition.

Fear is a socially contagious emotion[25] with a long evolutionary history[26]. Displays of fear and anger by other people are signals of the presence of immediate threat in the environment, and anger carries a clear intention to frighten the recipient. A plausible hypothesis is therefore that impaired recognition of fear and anger after amygdala damage reflects involvement of the amygdala in the appraisal of danger and the emotion of fear[12,13]. □

Methods

Audiometric testing used a DSP Pure Tone Audiometer, with separate testing of left and right ears at 250, 500, 1,000, 2,000, 4,000 and 8,000 Hz. D.R.'s thresholds were all at normal levels for her age, with 100% correct reports of 20-db sounds across the frequencies critical for speech perception (500–2,000 Hz).

Auditory processing of words and non-words (Table 1) was assessed using tests from the Psycholinguistic Assessments of Language Processing in Aphasia battery[14]; control data are taken from the test's norms. The other tests summarized in Table 1 (recognition of environmental sounds, interpretation of vocal expressions of emotion, unfamiliar voice matching and recognition of familiar voices) are described elsewhere[15]. D.R.'s performance is compared with that of 20 control subjects (10 men, 10 women) aged 40–59 years[15].

The emotional-words test (Table 2) involved 6 bisyllabic concrete nouns with neutral meaning (carpet, finger, hammock, motor, sailor, daughter). These nouns were selected to have varied phonetic properties. The initial phoneme was varied across two fricative onsets, two plosive, one aspirant and one nasal obstruent. Stress was held constant (on the first syllable) and each stressed syllable featured a different vowel.

These nouns were spoken by six native English speakers (3 male, 3 female, with a variety of accents), in five different manners intended to convey emotions of happiness, sadness, anger, fear or disgust. These emotions were chosen because they are each known to be associated with distinct sets of prosodic features[19]. Training and feedback were given to ensure that appropriate prosodic features were used to communicate each emotion. The speech was recorded in a sound-protected environment onto digital audio tape (DAT).

Tokens of each speech item were digitized at 22 kHz, and presented to 5 judges for categorization as each emotion. These categorizations were used to make up a set with ten different stimuli per emotion which resulted in similar average correct categorization of each emotion across the 5 judges (happiness, 82%; sadness, 93%; anger, 94%; fear, 89%; disgust, 84%). This selection was made subject to the constraint that at least one example of each word would be used for each emotion, and the different speakers should be used as evenly as possible (it was not possible to do this perfectly evenly across speakers: thus, there were 13 stimuli from each of three speakers, and 7 and 4 respectively from the other two).

For the test of emotion recognition from neutral-content words, the digitized tokens selected were presented in a random order using PsyScope software[27] running on a Macintosh Powerbook 540v computer and two loudspeakers set to a comfortable loudness level. Five additional items (one for each emotion) were used as practice trials. D.R.'s performance is compared to 10 controls aged 50–69 years (mean, 58.90 years; s.d., 6.59) without formal education.

Stimuli for the emotional-sounds test (Table 2) were recorded from two native English speakers (one male and one female), who were asked to generate a range of non-verbal sounds corresponding to the six basic emotions of happiness, sadness, anger, fear, disgust and surprise. This list was the same as that commonly used in work on facial expressions[1,5,28,29] to facilitate comparison. Sounds included: for anger, growls; fear, screams; happiness, laughter; sadness, sobbing; surprise, gasping; disgust, retching. The vocal expressions were recorded onto DAT in a sound-protected environment.

Tokens of the different vocal expressions were digitized at 22 kHz. In all, there were 27 angry sounds, 20 disgust, 24 fear, 27 happy and 31 sad sounds. These were presented to 6 judges for categorization. From their classifications, ten stimuli per emotion were selected so that the six emotions were recognized at similar overall levels (happiness, 90%; sadness, 87%; anger, 95%; fear, 93%; disgust, 97%; surprise, 93%).

For the test of emotion-recognition from sounds, the digitized tokens selected were presented in a random order using PsyScope software[27] running on a Macintosh Powerbook 540v computer and two loudspeakers set to a comfortable loudness level. Six additional items (one for each emotion) were used as practice trials, following which the test sounds were presented in a random order, with each stimulus presented twice across two blocks of trials. D.R.'s performance is compared to 12 controls aged 50–64 years (mean, 57.17; s.d., 3.88) without formal education.

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Correspondence and requests for materials should be addressed to A.W.Y. (e-mail: andy.young@mrc-apu.cam.ac.uk).

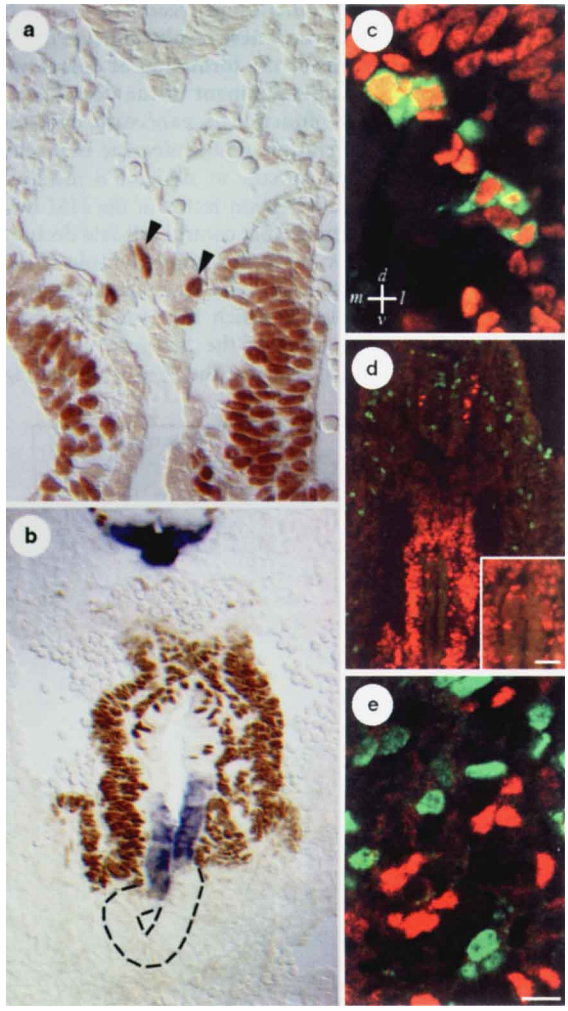

Figure 1 Expression of ISL1 in pancreatic epithelium and mesenchyme. **a**, In 16-somite embryos, ISL1$^+$ cells are detected in the dorsal pancreatic epithelium (arrowheads) and in the lateral mesenchyme. **b**, At the 25-somite stage, ISL1$^+$ mesenchyme has accumulated around the dorsal pancreatic bud. ISL1 is not expressed in the ventral pancreatic epithelium (broken line) or in the adjacent mesenchyme. *Shh* mRNA expression (dark blue) is used to visualize lateral endoderm[16]. **c**, Confocal image of the dorsal pancreatic bud of an e9.5 *Isl1*(+/+) embryo showing that all glucagon$^+$ cells (green) are also ISL1$^+$ (red). The image is representative of 5 embryos examined. **d**, No pancreatic epithelial cells in e9.5 *Isl1*(+/+) embryos are double-labelled with mpm2 (ref. 22) (green) and ISL1 (red) antibodies (insert) (n = 653 ISL1$^+$ cells analysed; 4 embryos). **e**, No ISL1$^+$ cells (red) incorporated BrdU (green) in explants of e12 dorsal pancreas cultured for 24 h and labelled with BrdU for 60 min to detect cells in the S and G2 phases of the cell cycle (n = 814 ISL1$^+$ cells; n = 1694 BrdU$^+$ cells analysed; 2 embryos). In **a**–**d**, dorsal epithelium is up. Scale bar in **a**, **d**, insert, 20 μm; in **b**, 40 μm; in **c**, **e**, 10 μm.

Independent requirement for ISL1 in formation of pancreatic mesenchyme and islet cells

Ulf Ahlgren*, Samuel L. Pfaff†‡, Thomas M. Jessell†, Thomas Edlund* & Helena Edlund*

** Department of Microbiology, University of Umeå, S-901 87 Umeå, Sweden*
† Howard Hughes Medical Institute, Department of Biochemistry and Molecular Biophysics, Center for Neurobiology and Behavior, Columbia University, New York, New York 10032, USA

The mammalian pancreas is a specialized derivative of the primitive gut endoderm and controls many homeostatic functions through the activity of its component exocrine acinar and endocrine islet cells. The LIM homeodomain protein ISL1 is expressed in all classes of islet cells in the adult[1,2] and its expression in the embryo is initiated soon after the islet cells have left the cell cycle. ISL1 is also expressed in mesenchymal cells that surround the dorsal but not ventral evagination of the gut endoderm, which together comprise the pancreatic anlagen. To define the role of ISL1 in the development of the pancreas, we have now analysed acinar and islet cell differentiation in mice deficient in ISL1 function[3]. Dorsal pancreatic mesenchyme does not form in ISL1-mutant embryos and there is an associated failure of exocrine cell differentiation in the dorsal but not the ventral pancreas. There is also a complete loss of differentiated islet cells. Exocrine, but not endocrine, cell differentiation in the dorsal

‡ Present address: Gene Expression Laboratory, The Salk Institute, 10010 North Torrey Pines Road, LaJolla, California 92037, USA