129P THE EFFECTS OF PRESSURE ON CELL SIGNALLING

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Pressure has a profound inhibitory effect on the ionotropic receptor for glycine that is entirely consistent with the pharmacologic analysis of the action of pressure *in vivo* (Roberts *et al.*, 1996). However, pharmacological experiments *in vivo* indicate that the neurological processes involving the metabotropic receptors for both dopamine (DA1 & DA2) and serotonin (5-HT1b, 5-HT2c) are also affected by pressure (Kriem *et al.*, 1996; 1998).

The aim of this study was to investigate whether pressure affects intracellular signalling processes.

The effect of pressure on an intracellular pathway involving Gq, PLC and IP3 activation, was studied by expressing receptors for the bacterial protein N-formyl-L-methionyl-L-leucyl-phenylalanine (fMLP) in *Xenopus* oocytes. Additional experiments tested the effect of pressure on oocytes stimulated with NaF; believed to directly activate Gs and stimulate AC. Oocytes (stage V) were injected with 50nl of mRNA solution (1µg/µl) and maintained overnight in modified Barth's medium containing penicillin (50 U/ml) and streptomycin (50 µg/ml) at 18°C to allow expression of receptors. Prior to use all oocytes were collagenase treated in Ca^{2+}-free Barth's to remove follicular and thecal cells. Receptor function was measured using two-electrode voltage clamp and an apparatus designed to fit in the pressure chamber (Roberts *et al.*, 1996).

Oocytes were perfused with frog Ringer (NaCl 120, KCl 2, CaCl2 2, Hepes 10; mM. pH 7.4) and clamped at -70mV for electrical recordings. Oocytes were stimulated by 30s perfusion with either fMLP (100nM) or NaF (40mM) in Ringer. Recordings were made at atmospheric pressure, and at 5 MPa and 10 MPa with pressure applied using helium.

Stimulation with fMLP produced a biphasic inward current. The fast component reversed at –25mV and was blocked by SITS suggesting it is carried by Cl^-. The slow component showed strong inward rectification, was Ca^{2+} dependent and blocked by Cd^{2+}, TEA and 4AP suggesting activation of a Kir channel. Stimulation with NaF produced a monophasic inward current that showed voltage dependence suggestive of a Na^+ channel. The fast conductance stimulated by fMLP was not affected by pressure; average currents relative to control were 0.69 +/- 0.17 (s.e.m.,n=5) and 0.90 +/- 0.34 (s.e.m., n=5) at 5 and 10 MPa, respectively. However, the slow conductance was inhibited by pressure; average relative currents 0.50 +/- 0.1 (s.e.m., n=5, Student's t-test p ~ 0.05) and 0.62 +/- 0.13 (s.e.m., n=5). In contrast, the slow conductance elicited by NaF is enhanced at pressure; average relative currents 1.54 +/- 0.3 (s.e.m., n=2) and 2.47 (n=1) at 5 and 10 MPa, respectively.

These results suggest that the modification by pressure of dopaminergic and serotonergic processes in vivo may arise from an action of pressure on intracellular signalling pathways and not on receptor-ligand binding or G-protein activation.

Roberts, R.J., *et al.* (1996) *Neurosci. Letts.*, **208**, 125-128.
Kriem, B., *et al.* (1996) *Pharmacol. Biochem. Behavior*, **53**, 257-264.
Kriem, B., *et al.* (1998) *Brain Res.*, **796**, 143-149.

130P AN INTERACTIVE MULTIMEDIA COMPUTER-ASSISTED LEARNING PROGRAM TO TEACH BASIC ANATOMY AND MECHANICAL FUNCTION OF THE RESPIRATORY SYSTEM TO MEDICAL STUDENTS

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The teaching of anatomy to medical students at the University of Edinburgh has undergone significant change in recent years: cadaver dissection has ceased and contact hours have been reduced by 75% with anatomy now being taught within an integrated systems approach. The multimedia program we describe here has been developed to support the teaching of respiratory anatomy and is designed as a resource for student-centred learning and tutorial teaching. The program was developed using Macromedia Director (version 7) for delivery on either PC (minimum specification: Pentium PC, Windows 95/98/NT4, 16 Mb RAM, 10 Mb available HD space, 16 bit colour graphics) or Macintosh (minimum specification Power PC, 16 Mb RAM, OS 7.5, 10 Mb free HD space, 16 bit colour graphics) platforms or potentially the Internet.

The program covers the basic anatomy and mechanical function of the respiratory system and is divided into several sections accessible from a menu:

- Chest Wall - bones (vertebrae, ribs, sternum), intercostal muscles, diaphragm (structure, nerve & blood supply), accessory respiratory muscles, visceral & parietal pleurae.
- Lungs - development of pleural cavity, pleural membranes, lung structure, blood supply, lymphatics, innervation).
- Nose and nasal cavity - structure, innervation, blood supply, sinuses, conchae
- Pharynx - wall, muscles, innervation, blood supply.
- Larynx - epiglottis, cartilages, control of the airway, vocal cords.
- Trachea - structure, blood supply, innervation.
- Bronchi - structure of bronchial tree, innervation.
- Alveoli - structure, cells (macrophages, pneumocytes).
- Breathing - diaphragmatic, animated movements of chest wall, animated radiographs.
- Speech - animated vocal cord movements.

High quality graphics (thumbnails which may be 'zoomed' for greater detail), diagrams, animations and videoclips (e.g. vocal cord movement) are used extensively to explain principles such as how the respiratory muscles and diaphragm interact to cause inspiration and expiration. There are also self-assessment questions attached to each section. Additional features include: a notes function (notes may be created as you work through the package, copied to the clipboard and pasted into a word-processing package or e-mail); an alphabetical index of structures which allow access directly to the relevant screen describing that structure.

The program is aimed at medical students and will occupy them for 3-4 hours of self-directed learning. It may also be suitable for other students e.g. physiotherapy.

131P THE OPEN CAMPUS: A DISTRIBUTED LEARNING GENERAL PHARMACOLOGY COURSE

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Most pharmacology programmes will have a unit of general pharmacology that covers the major principles of pharmacodynamics and pharmacokinetics. We have also taught these areas at the start of conversion postgraduate courses and short courses to industry for students without a pharmacology background. All of these groups could use in differing ways open/distributive material to support and/or provide the primary information source for a general pharmacology unit.

We are developing a computer based general pharmacology package for use by short course participants, and as open learning material for pharmacology students on traditional university courses. The majority of the package is web-based to run on a standard browser with the appropriate plug-ins and includes its own navigational aids for ease of use. Each part of the course is a self-contained unit that is intended to be viewed in a linear manner, but it is possible to jump to any point for purposes of revision and clarification.

Some might argue that, when using a different delivery system such as computers, the style of presentation must change drastically from that used in a traditionally taught university course. We have been influenced by feedback from our students and short course participants which has indicated a strong preference for standard lectures, seminars and workshops as the primary means of delivery of the taught material. Therefore, this computer-based course has attempted to reproduce as closely as possible the teaching programme used on campus, and for short courses delivered to industrial clients. PowerPoint presentations are presented on individual web pages, but significantly enhanced with animations and interactivity to hold the interest of the student. Each slide is accompanied by a voice-over that is very similar in style to the lecturer's presentation. Practical elements for the courses are provided by the use of simulations. This has been extensively used in the kinetics components where interactive models of drug kinetic processes provide instant feedback information and data to be analysed by the student. This presentation style combined with interactivity and ease of navigation offers the benefits of a conventional live presentation with the flexibility afforded by the new technologies. Throughout the sessions there are tests that maybe used for self-assessment, or the results can be sent to a tutor via e-mail. While the package is intended to be self-contained, e-mail contact, and possible on campus tutorial sessions, and 'wet' practicals would be available for further support.

We will be demonstrating the pharmacokinetics unit of this computer-based course that illustrates the interactions of the classroom lectures, the simulated practical sessions and the self-assessment tests. We will also be showing the component of the pharmacodynamics unit that covers G-protein-coupled receptors. An external examiner has critically evaluated some individual components of the computer-based course. Also pharmacology students have used parts of the programme, but the integrated package has yet to be evaluated. This evaluation will take place when the entire course can be offered via distance learning to participants off campus.

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132P NEW ANTIEPILEPTIC DRUGS

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New antiepileptic drugs (AEDs) are necessary for patients with chronic epilepsy and for improving upon established AEDs as first line therapy. Ten novel anti-epileptic drugs (AEDs) have been launched worldwide in the last decade. Six of these (in chronological order of appearance: vigabatrin, lamotrigine, gabapentin, topiramate, tigabine and oxcarbazepine) are currently available in the United Kingdom.

Complete freedom from seizures with the absence of side effects should be the ultimate aim for AED treatment and the new AEDs have not entirely lived up to expectations. Only a small number of patients with chronic epilepsy have been rendered seizure-free by the addition of new AEDs. Despite claims to the contrary, the safety profile of the new drugs is only slightly more favourable when compared with the profile of the established drugs. The chronic side-effect profile for the new drugs is yet to be fully established. Recently, one of the new AEDs, vigabatrin, has been associated with a chronic side-effect which has limited its use.

Most patients with chronic epilepsy still rely on the development of novel treatment for their only hope for seizure control. This is, however, a heterogeneous group and it is unlikely that a drug that is efficacious for all patients will ever be found. Another important reason for the continued quest for new treatments is the need for safer alternatives as none of the AEDs currently available, including the new ones, are free from adverse effects.