Editor's Note

J. Greg Anson

To cite this article: J. Greg Anson (1989) Editor's Note, International Journal of Neuroscience, 46:1-2, 1-40, DOI: 10.3109/00207458908991611

To link to this article: http://dx.doi.org/10.3109/00207458908991611

Published online: 07 Jul 2009.

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Editor's Note

The Sixth International Australasian Winter Conference on Brain Research was held, once again, in the delightful resort setting of Queenstown during the third week of August 1988. While snow conditions were just a little less than perfect, good skiing was experienced. This year a record number of abstracts was submitted and 68 which were accepted appear in this issue of the International Journal of Neuroscience. Again the multinational flavor of the meeting was well preserved. Although the majority of participants represented research programs in New Zealand and Australia, almost a quarter of the contributors came from farther afield including U.S.A., Japan, Germany, Sweden and Norway.

The interdisciplinary nature of the conference is one of its strong points and this year topics included Neurology, Vestibular–Oculomotor Mechanisms, Neuroanatomy and Plasticity, Neuropsychology, Regeneration, Psychopharmacology, Spinal Cord, Neurophysiology of the Hippocampus, Motor Control, Learning and Memory, Kindling and Epilepsy, Laterality, Anxiety, Motor Control Disorders and Vestibular System Plasticity. Lively discussion ensued at all sessions, leaving a distinct impression that interest and participation in neuroscience in the Southern Hemisphere continues to develop strongly.

Generous financial support from the New Zealand Neurological Foundation enabled many students to be assisted with registration and travel to the conference. Contributions were also received from the Mount Cook Line and Gordon and Breach, Science Publishers, Inc. The Seventh International Australasian Winter Conference on Brain Research will be held in Queenstown, New Zealand in August 1989.

J. Greg Anson
University of Otago
Collagenosis in Wallerian Degeneration Depends on Peripheral Nerve Type

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The aim of this study in the mature rat was to determine the extent of peripheral nerve collagenosis in response to Wallerian degeneration and to examine whether non-fibroblastic elements such as Schwann cells were important. Collagen was estimated as hydroxyproline content of normal and axotomized nerve fascicles after single or double crush lesions of both myelinated and unmyelinated nerves. Crushed unmyelinated nerve produced two to four times more collagen relative to control nerve than did the sciatic nerve. The nature of the interaction between the two successive crushes was different in the two nerves. These results suggest that the degree of collagen fibrillogenesis occurring in Wallerian degeneration is dependent on peripheral nerve type, and that the presence of myelin is not necessary for collagen fibrillogenesis.

Genetic Study of the Late-Onset Neuropathy of CBA T6/T6 Mice

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We have observed a syndrome to occur in the CBA T6/T6 inbred strain of mice (Adams et al., Proceedings University of Otago Medical School, 1987, 65, 27–28). In old age these animals become hyperactive, ataxic, lose weight and show priapism in the males. Unusual features of this syndrome are its abrupt onset and its universality. There is no sign of infection. White blood cell counts are normal. The nervous system is normal to light microsocopy. No vascular or other anatomical cause is apparent for the priapism. We suspect the syndrome has its basis in neurone death in certain brainstem nuclei. The priapism may be due to release of a spinal reflex from superior inhibition, analogously to the increased tendon reflexes resulting from upper motor neurone lesions. A further group of male and female CBA T6/T6 mice have been followed to old age. The syndrome has again occurred, with universal fall of weight from about 90 weeks of age and priapism starting at about 100 weeks to become universal by 120 weeks. This confirms the syndrome as an inherent characteristic of CBA T6/T6 mice. To determine the genetics involved, F₁ and F₂ hybrids have been bred with the NZW and C57/B1 inbred strains. Results indicate that the syndrome is recessively inherited and caused by multiple genes. The phenomenon may be an insight into a death clock governing life span.
Cortical Evoked Potentials (CNV) in Violent and Nonviolent Alcoholics

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Forty-eight male alcohol abusing patients were recruited among residents at the Hjellestad Clinic in Bergen, Norway. They formed subgroups high and low on alcohol-related violence. All subjects performed a laboratory task that permitted measurement of contingent negative variation (CNV) at the vertex of the skull. The paradigm represented forewarned (S1) ‘GO-NO GO’ reaction time tasks. In one version of the task S1 signals ‘GO’ (button press) in response to S2 which followed 3.5 seconds later. In contrast, in the ‘NO GO’ version, S1 signalled that no response was required to S2. In the ‘GO’ condition, subjects high in alcohol-related violence developed significantly greater negativity in the later half of the S1-S2 interval, compared with CNV responses given by the non-violent subjects. This group difference indicated that the violent drinkers were more cortically prepared for motor responding to S1 cues signalling ‘GO,’ whereas the two groups did not differ in their cortical changes over the first half of the S1-S2 interval. This meant they were equally efficient at allocating attention to the S1 signals. These results support a biological disposition for motor responding in violent alcoholics that may interact with drug effects in ways that explain their psychosocial problems.

Supported by a grant from the Norwegian Research Council for Science and the Humanities.

Sensory Input Regulation in Somatization Disorder

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Somatization disorder is a psychiatric condition characterized by the experience of multiple physical symptoms, often accompanied by pain, for which no organic medical reason can be found. Explanations of this disorder have traditionally been psychodynamic and sociological. Over a series of studies we have explored the possibility that somatization disorder is determined by a neurophysiological dysfunction in the processing of afferent stimuli. Our latest research examined sensory input regulation in terms of augmentation of auditory evoked potentials (AEPs) in response to tone-bursts of varying intensity. The phenomenon of augmentation reflects the central nervous system’s tendency to increase its response as the intensity of stimulation increases. In patients with somatization disorder the extent of augmentation, measured via the amplitudes of the P1-N1 components of AEPs, was larger than in a control group of normal subjects. This finding, which is consistent with those of our previous studies, suggests a disturbance in the central regulation of attention paid to afferent stimuli, and may help explain why somatization disorder patients suffer from a multiplicity of chronic physical symptoms.
CONFERENCE ON BRAIN RESEARCH

VOR Gain Depends on Target Distance

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The vestibulo-ocular reflex (VOR) stabilizes the direction of gaze during head rotation. Because the centers of rotation of the head and the eyes do not coincide, the eyes have to move faster than the head to maintain direction of gaze. A simple formula can be derived which describes this relationship. We have measured VOR gain in 6 subjects for different distances and shown agreement between theoretical and experimental data. Three male and three female subjects were studied. Subjects wearing a scleral contact lens and a head-fixed coil sat in a 2 meter³ magnetic field in darkness viewing a fixation light. The search coil system allowed measurement of head and gaze velocity accurate to within 3 deg/s. Following extinction of the fixation light the subjects head was passively moved right or left at a velocity up to 250°/s. Head and gaze velocity was sampled at 600 Hz. VOR gain (Eye/Head velocity) was calculated for 6 different fixation distances. About 20 head movements were processed for each fixation distance. While individual differences are apparent there is general agreement between the theoretical and experimental data in that VOR gain is greater than 1.0 when the fixation light is close to the eye and drops to about 1.0 at 1 m. The hypothesis that VOR gain is mediated by vergence is consistent with these data.

Analysis of the Saccadic Control System using Double-Step Stimuli: Application of Parametric and Nonparametric Mathematical Models

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Shifting the location of a visual target (S2) at some time prior to or during a previously invoked saccadic eye movement has provided the means for a more thorough investigation of the motor control processes involved. Generally at short interstimulus intervals (ISI) reaction time (RT2) to S2 is increased compared to the latency (RT1) of the first saccade; the initial saccadic amplitude (SA1) may also be modified. At longer ISIs the interval (IRI) between the two saccadic responses is increased. However, data resulting from the application of this experimental paradigm display large inter- and intrasubject variability. Even when variability in initiating the first saccade is controlled for, by plotting each datum as a function of shared processing time of the two stimuli, the data are not equally spaced or distributed. Traditional methods of analysis that involve averaging data between individuals and fitting curves to individual data 'by eye' have tended to mask important trends and have been prone to subjective biases. In contrast, our approaches involve the application of parametric and nonparametric mathematical models to individual data and provide a more objective and sensitive method of analysis. This paper compares and contrasts these methods of analysis and shows how the application of mathematical models furthers our understanding of saccadic control processes by revealing important response signatures that are sensitive to stimulus parameters and cognitive function.
The Effect of Repeated Exposure to a Moving Visual Field on Perception of Self-Motion and Optokinetic Nystagmus

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If a subject is seated inside a drum filled with black and white vertical stripes, when the drum is rotated the subject experiences illusory self-motion in the opposite direction to the drum rotation. This illusion, known as circular-vection (CV), is a powerful demonstration of the integration of visual and vestibular information in brainstem and cortical vestibular neurons. Typically, CV begins within 5-10 s of the onset of drum motion, and is associated with optokinetic nystagmus (OKN) with a slow phase in the direction of the drum motion. We investigated the effect of repeated exposure to the moving visual field on latency to CV and frequency of OKN (recorded with EOG electrodes). Subjects were seated inside a 2 m (diameter) optokinetic drum filled with vertical black and white stripes (of 2° and 4° width respectively), which was rotated at a constant velocity of 50°/s. Subjects were exposed to the optokinetic stimulus for 6 30-s periods, separated by 1 minute intervals of darkness, and were required to press a button as soon as they experienced CV. The button press stopped a digital timer which provided a measure of latency to CV. Over the 6 trials, the latency of CV decreased, suggesting an increased sensitivity to the illusion. The decreased latencies did not seem to be due to an increasing aftereffect in the intertrial intervals nor to practice at the task. The relationship between this reduced latency to CV and OKN will be discussed.
The Experience of Oscillopsia: A Case of Familial Nystagmus

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Oscillopsia has been defined as an 'optic illusory movement of a viewed stationary target.' (Bender, 1965, Archives of Neurology, 13, 204–213). This perceptual experience is often, but not always, associated with a blurring of the visual image. Although many descriptions exist of the examination findings associated with oscillopsia, little significance has been given to what the patient with this symptom experiences and how it affects their daily life. We present data from a 47 year old female with a 30 month history of oscillopsia on downward gaze associated with vertical nystagmus and mild ataxia. Her experience of oscillopsia is reported and discussed. The patient's mother and three sisters all experienced similar visual symptoms, and mild ataxia was reported. A diagnosis of familial spinal-cerebellar degeneration is suggested and possible neurophysiological mechanisms for this type of oscillopsia are discussed.
Rhodamine Labelling of Small Numbers of Neurons in Mammalian Nerves

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To assess the sprouting of regenerating axons and the path taken by them, we have developed a method which allows the tracing of restricted numbers of axons using the fluorochrome rhodamine. Under anaesthesia, a few crystals of rhodamine B isothiocyanate are inserted into the nerve of interest: e.g., the sciatic nerve in rat and rabbit, the sternomastoid nerve in the rat, rabbit cornea sensory nerve branches. Sixteen to 18 hours later, the labelled tissue was excised and fixed. Sections of larger nerves and spinal cord, or whole mounts of corneas and smaller nerves were examined using fluorescence microscopy. The method allows for discrete labelling of a small number of axons over lengths of at least 20 mm both proximal and distal to the labelling site. Cell bodies were also labelled. In nerve grafts, or severed and reanastomosed nerves, axons can be traced through the anastomosis or graft, and at short recovery times, many fine sprouts can be observed. At longer recovery times, branches are relatively rare at an anastomosis, although the axons often follow tortuous pathways. Many of the small branches, although well labelled, are difficult to photograph because they are small and produce only low levels of fluorescence, and because they travel in and out of the plane of focus. Image intensified video recording will probably be required for large scale quantification.

Stereological Determination of the Extent and Nature of Synaptic Plasticity in Aging Rat Neocortex

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Remodelling and turnover of synapses in the postdevelopmental neocortex is implicit within the process of synaptic plasticity. Perforated synapses (PSs) are one of several morphological types of synapse identified within the mature brain. Previous data suggested PSs are involved as structural intermediates in synaptic plasticity; the precise mechanism of their involvement is unknown. However, some indication of the extent and nature of synaptic remodelling and turnover, throughout life, may be given by changes in the number and morphology of PSs. The numerical density and frequency of PSs in aging rat neocortex were estimated using an unbiased stereological method [Disector]. The morphologies of PSs were also compared. Nine groups of male rats aged from 0.5 months to 22 months were studied. It was found that the mean numerical density of PSs increased 110% between 0.5 and 10 months of age (paired t-test; p < .05). This decreased 39% during the 10 to 22 month period (p > .05). The frequency of PSs increased 99% between 0.5 and 10 months (p < .05) but declined 28% between 10 and 22 months (p > .05). Spatial configuration, and ultrastructural changes, were also observed throughout the 21.5 month study period. The changes observed may reflect a reactive response to the increasing demands imposed on aging
animals which may be necessary for their survival. These data suggest that synapses within the mature brain are considerably more plastic than has previously been thought.

Three-dimensional Reconstructions Reveal Changes in the Spatial Configuration of Perforated Synapses in Aging Rat Neocortex

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Synaptic plasticity is a naturally-occurring process which is of fundamental importance in the functioning of the mature brain. Perforated synapses (PSs) are thought to be involved in this process as intermediate structures. A study of the unique morphological characteristics of PSs can only be effectively achieved by three-dimensional reconstruction of their serial section images. As part of a parallel investigation, reconstructions were made of selected PSs from the parietal cortex of nine groups of male rats aged from 0.5 months to 22 months. A specifically developed computer package was used which permitted semiautomatic reconstruction of these connections using an Apple Macintosh Plus microcomputer and Imagewriter I1 printer, with a Houston Instruments HIPAD EDT11 digitizing tablet with cursor. The program contained a section fitting routine and provided a choice of reconstruction parameters and drawing options. It was found, over the 21.5 month time course, that: (i) the active region, and its perforations(s), increased considerably in size; (ii) overall postsynaptic shape changed from being 'negatively curved' (concave with respect to the postsynaptic terminal) to being 'positively curved,' and (iii) perforations changed from simple discrete 'holes' to having highly complex configurations. The reconstructions clearly demonstrate the relationships between the characteristic morphological features of PSs. This will facilitate our understanding of their role in synaptic plasticity.

Assessment of Axonal Sprouting Across a Single Anastomosis in Mammalian Peripheral Nerve

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The number of sprouts a single axon contributes to the nerve stump distal to an anastomosis was investigated in the rat. Under anaesthesia, the tibial or peroneal branch of one sciatic nerve was cut and anastomosed microsurgically. At various recovery times, myelinated and unmyelinated axons were counted and measured using electron microscopy. Nerve section initiated a proliferation in the number of axons in the proximal and distal stumps, suggesting that the severed axons produced numerous sprouts. At 12 weeks, the number of axons in the proximal stump remained greater than control. However, there was a substantial reduction in axon numbers in
the distal stump to approximately 80% of that in the proximal stump. At two weeks, nonmyelinated axons comprised 99% of the population of axons; by week 12, they comprised 63% of the total population. A sharp drop in total number of axons during week 4 was associated with a substantial decrease in nonmyelinated axons. Data on axon diameters and myelin thickness suggest that myelination of the largest nonmyelinated axons coincided with the disappearance of many others. The drop in the total number of axons must result from a reduction in the number of sprouts the proximal axons initially generate. Labelling of individual axons with rhodamine (RITC) indicated most axons lose all but one process by the end of week 16.

### The Effect of Proximodistal Orientation of Peripheral Nerve Grafts on Axonal Regeneration

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Peripheral nerve transplants, used for surgical repair of nerve loss, are normally implanted with the proximal–distal orientation of the graft maintained. If grafts contain branches, regenerating axons may be lost into them, limiting reinnervation and restoration of function in the denervated area. Since axons entering a reversed graft could not be lost in this way, we are investigating whether reverse implantation could enhance the number of axons which successfully navigate through a graft. In young adult rats, a section of sciatic nerve was removed, and a 1 to 2 cm autograft, including one major branch, was inserted with either the normal or reversed proximodistal orientation. After signs of return of function, the animals were perfused, and the operated and contralateral unoperated nerves of each animal were processed for electron microscopy. Serial thick and thin sections were subsequently examined by light and electron microscopy. Axons do enter branches in normally orientated grafts, and there is a substantial loss in the cross-sectional area of the graft distal to the branch termination. In two of three preparations for which axon counts have been completed, this is associated with fewer axons in the distal stump than in the proximal stump. Reverse grafts appear as well reinnervated by regenerating axons as normally orientated grafts, and do not show loss in the cross-sectional area. In five preparations, there were more axons in the distal stump compared to the proximal stump.

### Neonatal Denervation Triggers Synaptogenesis in the Ineffective Spinal Terminations of Single Cutaneous Afferent Fibres

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Previously we have demonstrated that single cutaneous afferent fibres have terminations in the dorsal horn that (a) do not appear to excite spinal neurons and (b) lack synaptic boutons (Meyers & Snow, 1984, *Journal of Physiology*, 347, 59-73). Denervation of toe 3 results in a reorganization of the somatotopic representation of toes 2
and 4 in a manner that is compatible with the conversion of the ineffective terminations of afferents supplying these toes, to an effective state (Wilson & Snow, 1987, Journal of Neurophysiology, 57, 803-818). In the present study we chronically denervated toes 3 and 4 of neonatal cats and then at adulthood mapped the representation of toes 2 and 5. This showed that the skin of toes 2 and 5 had established an excitatory influence over the deprived (toe 3 and 4) region of the map. In the same animals we intracellularly stained single cutaneous afferents that supplied toes 2 and 5 and found that some of these afferents had many synaptic boutons in the deprived region. The results show that removal of input to an area of dorsal horn is a sufficient stimulus to elicit synaptogenesis in the ineffective terminations of intact afferents that supply skin adjacent to the denervated area. We suggest: (a) that these ineffective terminations are a common though undetected feature of CNS organization and, (b) that they bestow upon the CNS the property of structural plasticity in a manner that does not violate localization of function.

Supported by the NH and MRC

**Plasticity in Frog Spinal Cord: Wiping Reflexes and Cord Surface Potentials after Regeneration of Cutaneous Nerves**

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Tactile stimulation of frog skin elicits accurately aimed wipes. When lateral nerves are redirected microsurgically to reinnervate dorsal skin within a dermatome, wipes are dorsally directed (Schrameck, J.E., 1973, Proceedings of the Australian Physiological and Pharmacological Society, 4, 181), a result suggestive of central synaptic reorganization. Experiments were performed to determine if, when posterior nerves are redirected to innervate anterior dermatomes; (1) plasticity occurs and (2) whether the distribution of dorsal root-evoked spinal cord surface potentials changes after reinnervation. Posterior nerves reinnervated anterior skin and spread to adjacent dermatomes. Some correctly aimed wipes were elicited from anteriorly located receptive fields of regenerated posterior nerves. In contrast to the result obtained with intradermatomal cross-innervation, most wipes were misdirected, but not to the segment of origin of the regenerated nerve. Many anteriorly directed belly wipes were elicited in response to stimulation of posterior dorsolateral skin. Normal wipes were obtained from undisturbed skin surrounding the operated skin area. Cord potentials peaked in the stimulated segment and declined over several segments. Distributions of cord surface potentials in operated animals resembled those in control frogs. These results may be due to sprouting of central processes or dorsal root ganglion cells, or activation of formerly quiescent synapses after reinnervation of foreign skin, or multiple innervation followed by central suppression of inappropriate synapses.
Lund and coworkers have shown that embryonic retinal tissue from both rats and mice (order Rodentia), when transplanted to the midbrain of neonatal rats, differentiates and develops connections with the host rat brain. We have repeated these experiments using fetal rabbit retina (order Lagomorpha) as the donor tissue. Retinae from fetal rabbits on postconceptional day 16 were dissected out and transplanted to a position either above the left superior colliculus or into the cerebral aqueduct of newborn rat pups. After survival times ranging from 8 to 64 days the host animals were perfused, the brains processed for Nissl and neurofibrillar staining. Over 70% of the transplants survived and differentiated into a laminar organization typical of normal retina. This observation together with the apparent lack of macrophages suggests that the transplanted tissue developed free of immunological constraints. Cells of the size and morphology of ganglion cells were present in the ganglion layer, and labelled ganglion cells were found within transplants following HRP injections into the superior colliculus. Several transplants located above the midbrain had developed a bundle of axons resembling an ‘optic nerve’ passing into the caudal section of the deafferented superior colliculus. Some retinae located within the cerebral aqueduct issued axon bundles dorsally into the denervated colliculus. These findings suggest that some of the factors influencing the survival of retinal ganglion cells and their axons are homologous between different orders of animals.

An Immunopathological Study (LM and EM) of Rejected Nerve Allografts in the Rat

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The number of Helper–Inducer T lymphocytes (T4+ cells), Cytotoxic–Suppressor T lymphocytes (T8+ cells), and macrophages, were quantified in peripheral nerve allografts from 1 to 14 days after implantation. Grafts were also tested for the expression of major histocompatibility complex (MHC) Class I and Class II molecules. The indirect immunoperoxidase method for light and electron microscopy was used. Dark Agouti rats served as the donor for allografts; Wistar rats were recipients, and also donors of autograft controls. There was a gradual but steady increase in the number of Helper T cells and Cytotoxic T cells between day 3 and day 6 postoperatively. The number of macrophages increased more slowly over that time. Between day 6 and day 7 there was a marked increase in the number of Helper and Cytotoxic T lymphocytes and macrophages, suggesting that this may be a critical time for T-cell and macrophage proliferation. Macrophages become the most common invading cell-type between day 7 and day 14. The results are consistent with the rejection pattern observed in other tissue allografts. Schwann cells were found to express MHC Class I and Class II molecules by day 2 postoperatively, which is well
before there is any substantial T-cell and macrophage infiltration. It may be that the donor Schwann cells act as antigen presenting cells, triggering the immune response and finally becoming a target of the rejection process.

Frontal Lobe Functions in Child Psychiatric Disorders

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In a departure from observations on cognitive task performance and cerebral activation patterns in certain groups of child psychiatric patients, functions of the frontal lobes were investigated by means of a multilevel study on 8- to 16-year olds with and without psychiatric disorders. Clinical groups being examined in this ongoing project (hyperactive children, anorectics, and children with tics) were compared against age- and sex-matched normal controls, and with a sample of children with confirmed isolated frontal lobe damage. Eventually, data form 120 normal controls and 24 subjects in each clinical group will be analyzed. Subjects with psychiatric disturbances will be reexamined as their clinical condition improves, to gain longitudinal information on how treatment effects influence psychopathology, cognitive abilities, and neurophysiological parameters. Data collected belong to different categories: neurophysiological (clinical evaluation of the EEG; frequency power spectra; evoked-potential paradigms); neuropsychological (divergent thinking; general and specific intellectual abilities; accuracy of intra- and cross-modal time reproduction; Continuous Performance Test, Wisconsin Card Sorting Test, Stroop color-word interference test); clinical assessment (structured neurological examination; parent and child interviews and questionnaires on familial and socioeconomic background, psychosocial risks, and psychopathological symptoms). According to our basic assumption, a child's ability to utilize frontal lobe resources is expected to play an important role in predicting course and outcome of the psychiatric disorder.

Supported by the Deutsche Forschungsgemeinschaft.

The Effect of Closed Head Injury on Linguistic Function in Children

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Few studies have investigated in any detail speech–language deficits following closed head injury in children (Ewing-Cobbs, et al., In M. Ylvisaker (Ed.), 1985, Head Injury Rehabilitation: Children and Adolescents, 71–89). In particular, the development of a comprehensive profile of speech–language abilities during recovery stages has not been attempted. In the present study, the speech and language functioning of a group of 20 children (aged 5–13) who had sustained a closed head injury were assessed with the purpose of developing a comprehensive profile of the type and severity of the long term speech and language disorders exhibited by this group. The subjects were administered a battery of speech–language assessments including: articulation–
phonologic assessment; oromotor assessment; overall language test; specific language skills assessment; and a pragmatic skills assessment. The profile of the speech-language impairment is outlined and the performance of the head injured group on the various speech-language tests compared to a group of non neurologically impaired accident victims matched for age, sex and socio-economic status. Results indicate that the closed head injured group present with subtle language deficits which are not identified through routine screening procedures.

Aphemia Associated with Bilateral Striatocapsular Lesions Following Acute Cerebral Anoxia

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The term ‘aphemia’ has been used to describe the isolated loss of the ability to articulate words without loss of the ability to write or comprehend spoken language (Albert et al., 1981, Clinical Aspects of Dysphasia). A distinct clinical pattern of aphemia has been identified. The patient presents initially as mute, most often acutely, and is temporarily unable to express himself vocally. The aphemic patient, however, is able to use written language to express ideas (Shif et al., 1985, Archives of Neurology, 40, 720-727). Previous reports in the literature have indicated that aphemia is usually associated with small lesions that either involve the cerebral cortex in the region of the pars opercularis or inferior precentral gyrus and/or the frontal subcortical fibre systems deep to the frontal operculum. No previous reports have appeared in the literature which document the occurrence of aphemia following large bilateral lesions of the striatocapsular region. The purpose of the present paper is to report such a case following cerebral anoxia and to discuss its implications for current theories regarding the role of the basal ganglia in speech-language functions.

Classical Vs. Atypical Antipsychotics on Oral Movements and GABA Turnover in Rats

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Two experiments were performed to investigate the effects of the butyrophenone melperone on vacuous chewing movements (VCMs) in a rat model for tardive dyskinesia (TD) and GABA turnover in rat substantia nigra. Chronic administration of antipsychotic drugs has been shown to increase the frequency of VCMs in rats. These changes seem to occur only in response to classical cataleptogenic neuroleptics, but not to the atypical antipsychotic clozapine. In the present study the effects of melperone were compared with those of haloperidol. As with clozapine, there are remarkably few reports of TD connected with melperone. Rats received therapeutically equivalent doses of either haloperidol or melperone continuously with their drinking water for 18 months. Treatment with haloperidol caused a dose-dependent
rise in VCMs, while melperone over a wide dose-range did not differ from untreated controls. In the second experiment the effect of melperone, clozapine or haloperidol on GABA accumulation after local infusion of the GABA-T inhibitor, gamma-vinyl GABA, into rat substantia nigra (SN) was compared after acute or chronic administration. According to the GABA hypothesis for tardive dyskinesia a chronic depression of striatonigral GABA neurons induced by classical neuroleptics eventually leads to irreversible damage of nigral GABA function. Atypical antipsychotics may not have similar effects on the nigral GABA system. The present study was conducted to determine whether melperone follows the pattern of typical or atypical neuroleptics in terms of changes in GAD activity in the SN. While clozapine and melperone did not induce significant alterations, haloperidol caused a reduction of nigral GABA accumulation (acute exp. -70%, \( p < .0004 \); chronic exp. -29%, \( p < .02 \)). The present results suggest that melperone might be classified with the group of antipsychotics which may be low-risk drugs with regard to extrapyramidal side-effects including tardive dyskinesia.

An Investigation of Behavioral Effect of Antichick Thy-1 Antibody

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Chicken Thy-1 was first purified from chicken forebrain (Rostas et al., 1983). Although the function of Thy-1 remains unknown, its abundance and expression in the mammalian and the avian nervous systems suggests that this molecule plays a prominent role in cell interaction and communication (Morris, 1985). Previous studies have shown that both polyclonal and monoclonal antibodies to chick Thy-1 inhibit long term memory (LTM) formation in neonatal chickens trained on a single trial passive avoidance learning task. We report here the results of studies on memory inhibition using monoclonal antichick Thy-1 IgG purified on DEAE-cellulose. (Fab')2, Fab and Fc fragments prepared from this monoclonal antibody were also tested. Bilateral administration of purified antichick Thy-1 IgG into the forebrain of chicks shortly after learning inhibited LTM formation when compared with control applications of physiological saline. A dose response study indicated that a high concentration of the IgG (20 \( \mu \)g–chick) is necessary for producing the inhibitory effects. Low doses of IgG showed variable results. Results of further experiments using (Fab')2, Fab and Fc fragments reveal that (Fab')2 and Fab were able to inhibit LTM. No effect was observed with the Fc fragment of this monoclonal IgG. Therefore, these results indicate that an amnestic effect appears to be mediated via the antigen binding sites of this IgG molecule. These results confirm and extend previous findings on the putative role of glycoproteins in memory formation.
Ultrastructural Localization of Lectin Binding within the Superficial Dorsal Horn of the Spinal Cord

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In the rat and cat, the plant lectin Soybean Agglutinin (SBA) binds to small diameter dorsal root ganglion cells and to the superficial laminae of the dorsal horn of the spinal cord (Plenderleith et al., 1988, Neuroscience Letters, 86, 257–262). Following dorsal rhizotomy, SBA binding in the superficial dorsal horn is abolished. These results are consistent with SBA binding to a subpopulation of unmyelinated primary sensory neurons (C-fibres). In the present study we have extended our analysis of SBA binding in the dorsal horn to the level of the electron microscope. In both the rat and cat, SBA binding was found to be associated with terminal varicosities within laminae I and II of the dorsal horn. SBA labelled profiles characteristically formed axodendritic synapses with small and intermediate sized dendrites. SBA binding was found to be restricted to the plasma membrane of labelled terminals. These results indicate that SBA is a convenient histochemical marker for C-fibre terminals at the ultrastructural level. Particularly interesting is the observation that SBA binding is limited to the plasma membrane of terminal boutons. It is known that antibodies raised against various putative neurotransmitters exhibit cytoplasmic rather than membrane binding. Using this difference in ultrastructural localization of binding we are currently attempting to combine SBA labelling of C-fibre terminals with immunocytochemistry to determine which substances modulate transmitter release from C-fibre terminals.

Supported by the NH & MRC

The Coexistence of Neuropeptides in the Soma and Central Terminals of Primary Sensory Neurones

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Immunocytochemical studies in our laboratory have shown that up to four, and possibly more neuropeptides may coexist within a single dorsal root ganglion (DRG) cell (Leah, et al., 1985, Neuroscience, 16, 683-690; Cameron, et al., in press, Neuroscience). Using a combination of intracellular staining and immunocytochemistry we have found no obvious correlation between the modality of a DRG cell and the peptides it contains (Leah, et al., 1985, Neuroscience Letters, 56, 257–263). However the possibility still remains that multiple peptide coexistence is a feature of the cell body and that a single peptide is expressed at the central terminals of the cell. In an attempt to address this question directly we have screened single synaptic boutons within the superficial laminae of the dorsal horn in the rat for the presence of substance P (SP) and Calcitonin Gene-related Peptide (CGRP). Serial ultrathin sections of rat dorsal horn were incubated in antisera against SP or CGRP and antibody binding sites were visualized on the electron microscope using a protein.
A-gold conjugate. A high level of coexistence of SP- and CGRP-like immunoreactivity was found in single synaptic boutons within the superficial laminae. It would appear then, that the level of peptide coexistence observed in a DRG cell is reflected in the central terminals of that neuron.

Supported by the NH and MRC.

Light and Electron Microscopic Studies on the Distribution of GABA and Benzodiazepine Receptors in the Dorsal Horn of the Human Spinal Cord

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There is considerable evidence suggesting that benzodiazepines (BZ) act via the GABA receptor complex. In particular, animal studies suggest that in the spinal cord, benzodiazepines act by enhancing GABA-mediated presynaptic inhibition on primary afferent terminals. In these studies the distributions of GABA and BZ receptors (BZR) in the human lumbar spinal cord have been compared at the light and electron microscopic levels using immunocytochemical methods and monoclonal antibodies to GABA and to the α- and β-subunits of the BZR complex. The results showed that at the light microscopic level there was a similar distribution of both GABA and BZR immunoreactivity in adjacent sections from the human lumbar spinal cord. There was an intense band of both GABA-immunoreactivity and BZR-immunoreactivity within lamina II of the dorsal horn with lower levels of staining in adjacent laminae. On electron microscopic examination, GABA immunoreactive cell bodies, dendrites and axon terminals were found within lamina II. In particular, GABA immunoreactive axon terminals were found contacting labelled and unlabelled axon terminals and dendrites. In adjacent sections processed for BZR immunoreactivity, intense immunoreactivity was seen on both the pre- and postsynaptic membranes of axodendritic and axoaxonic synapses. These results from light and electron microscopic studies on the human spinal cord are consistent with animal studies suggesting that benzodiazepines act at the GABA receptor complex.

Measurement of Neuropeptide Release in the CNS with Antibody Microprobes

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Antibody microprobes are fine glass microelectrodes coated with specific antibodies to a particular neuropeptide. They can detect nanomolar concentrations of neuropeptide released in the CNS by means of an in situ solid phase radioimmunoassay. This technique has localized the release of substance P to the substantia gelatinosa of the cat spinal cord in response to noxious cutaneous stimuli (Duggan et al., in press, Brain Research). The tips of glass microelectrodes were coated with an amino-silane polymer and then sequentially incubated in glutaraldehyde, Protein A and an antibody
directed against somatostatin, calcitonin gene-related peptide (CGRP), met-enkephalin-arg^5^-phe^7^ (MEAP) or dynorphin A. Using extracellular recording as an indication of electrode placement and neuronal excitability, microprobes were inserted into the lumbar cord of barbiturate-anesthetized cats with a spinal transection (L,) during cutaneous stimulation of the ipsilateral hind paw. Upon removal from the cord, microprobes were incubated in the appropriate radiolabel and then exposed to X-ray film. The resultant images were scanned by video camera and the optical density analyzed by computer. Localized deficits in binding were interpreted as sites of release of the neuropeptide in vivo. A basal release of somatostatin and CGRP from the substantia gelatinosa was present in the absence of cutaneous stimuli. Noxious mechanical stimulation increased CGRP release whereas noxious thermal stimulation increased release of both CGRP and somatostatin. In contrast, MEAP showed no release from the substantia gelatinosa with any of the stimuli tested. A basal release of dynorphin A was detected only with an intact spinal cord, suggesting a supraspinal control of dynorphin release. Since this technique is capable of assessing the dynamic status of a particular peptidergic pathway in the CNS, it will prove to be a valuable tool for neuropeptide research.

**LTP Conditioning Applied Antidromically Induces Long-Term Depression in CA1 Cells**

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If 6 bursts of 50 stimulus pulses at 10s intervals are delivered to the Schaeffer collateral-commissural pathway, long-term potentiation (LTP) of excitatory postsynaptic potentials (EPSPs) from that pathway on CA1 neurons will result. We have found, using intracellular recording in hippocampal slices, that if the same pattern of stimuli is delivered antidromically to the CA1 cells through their axons, a long-term depression (LTD) of the Schaeffer collateral-commissural EPSPs will result. LTD can be elicited if the conditioning stimuli are delivered in the presence of 25 mM Mg\(^{2+}\) and is thus not longlasting feedback inhibition nor a special case of heterosynaptic depression, (though it may underlie the mechanism of heterosynaptic depression). If, as is widely supposed, LTP is involved in learning and memory, then LTD must also be taken into account when considering the mechanisms of these phenomena.

**Reticular Elicitation of Hippocampal Rhythmical Slow Activity: Effects of GABA-agonists**

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Hippocampal rhythmical slow activity (RSA or theta) can be elicited by stimulation of the midbrain reticular formation. All classes of anxiolytic drugs reduce the fre-
frequency of reticular elicited slow waves. It has been proposed that some anxiolytics have their effects by acting as agonists of the inhibitory neurotransmitter GABA. In the present study a GABA-\(_A\) agonist, muscimol, and a GABA-\(_B\) agonist, baclofen, were injected into freely moving rats. Dose response curves for both drugs were obtained. Baclofen produced a decrease in frequency, an effect which increased with increasing dose. Muscimol produced an increase in frequency with an inverted U-shape dose response curve. Maximum effects were obtained on this test at a dose of 0.001 mg/kg. If anxiolytic drugs are acting as agonists of GABA, it appears they must do so through GABA\(_B\) receptors and not GABA\(_A\).

**Cysteamine Potentiates Entorhinal Activation of Dentate Gyrus Granule Cells in Rats**

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In the dentate gyrus of the hippocampus, a dense plexus of somatostatin (somatotropin releasing inhibiting factor) positive fibres and varicosities is contained in the outer two-thirds of the molecular layer where the entorhinal afferents (via the perforant path) terminate. These fibres are thought to originate at the hilar interneurons. This anatomical organization suggests an interaction between the entorhinal input and the somatostatin system in the dentate gyrus. To test this we injected pentobarbital anesthetized rats with cysteamine (200 mg/kg, i.p.) and tested its effects on perforant path evoked potentials. Cysteamine rapidly lowers somatostatin levels via a combination of an increase of release and an inhibition of synthesis. Cysteamine administration lead to an 109% increase in the population spike height (PS) elicited by perforant path stimulation within 30 min while the population excitatory post-synaptic potential (EPSP) was left unchanged throughout the experimental period (4 hours). Over a range of test pulse intensities, the PS showed a linear correlation with the associated EPSP. The slope of this relation showed a significant increase (46%) after cysteamine administration, but the x-intercept did not change. The antidromic population spike, evoked by mossy fiber stimulation and recorded in the dentate gyrus, was not changed by cysteamine when the perforant path evoked orthodromic PS was augmented. Four hours after cysteamine injection, the increase of PS tended to return to the predrug level. Lower doses of cysteamine (10 and 100 mg/kg) showed similar but smaller effects on the PS and the slope of its relation to the EPSP. These results, combined with other recent reports, suggest that cysteamine potentiates the entorhinal activation of dentate granular cells without affecting general cell excitability, and that the effects of cysteamine are due to an enhanced release of somatostatin.
Possible Relation Between Long-Term Potentiation and c-fos Induction in the Rat Dentate Gyrus

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It has been proposed that c-fos and/or other DNA binding proteins may act as 'third messengers,' i.e., intermediary agents governing the gene expression response to particular patterns of neural activity. The c-fos gene has recently been shown to be induced in neurons under a variety of depolarizing conditions, including following seizure or multiple spiking episodes. Here we tested whether c-fos induction accompanies the long-lasting synaptic strengthening (long-term potentiation, LTP) that is produced in the rat dentate gyrus by perforant path tetanization. Unilateral high-frequency (400 Hz) stimulation in unanesthetized rats produced LTP ipsilaterally and increased the number of c-fos protein immunohistochemically-positive dentate granule cells per 100 μm² by 89–367%, compared to the contralateral nontetanized dentate gyrus. The change in staining was observed 30 min and 4 hr, but not 10 min or 24 hr following tetanization. The NMDA receptor-channel antagonists CPP and MK801, plus the anesthetic urethane, reduced LTP and c-fos staining. Low frequency (1 Hz) stimulation in awake rats induced neither LTP nor c-fos. In other animals, a large increase in c-fos messenger RNA (Northern blot technique) was seen in the ipsilateral hippocampus 30 min following LTP induction. Thus, nonseizure producing stimulation in the perforant path can elevate c-fos messenger RNA and protein products postsynaptically in the dentate gyrus of awake rats, but the precise relation between these changes and LTP remains uncertain.

Reflex Control of Joint Stiffness in Human Subjects

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Electromyographic activity was recorded from elbow flexor and extensor muscles in human subjects while irregular force perturbations were applied to the elbow joint. On-line feedback of muscle contraction levels was displayed to the subject, who was instructed to make the elbow either 'stiff' or 'compliant' while maintaining comparable contraction levels in the muscles. Box-Jenkins transfer function modelling of the
dynamic relationship between the applied torque and the resulting elbow angle showed that the mechanical impedance of the elbow joint is equivalent to an inertia with viscous and stiffness elements. The stiffness of the joint was reduced more than 4-fold between the 'stiff' and 'compliant' conditions, despite comparable or higher contraction levels in the muscles in the compliant condition. On the other hand, tonic stretch reflexes (TSRs) in the elbow muscles, computed by the Box-Jenkins technique, showed significant reversals in phase and reductions in gain in the 'compliant' compared to the 'stiff' condition. The computed transfer functions indicate that the TSRs can be adequately modelled by three parallel loops with short (0–25 ms), medium (25–75 ms) and long (75–125 ms) latencies, whose loop gains can be varied independently of the muscle force and length.

Visual Control of Targeted Forces and Movements of the Human Arm

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Targeted forces and movements of the human arm are thought to be controlled by centrally organized motor commands and then modified by visual input. Although it is frequently presumed that rapid force changes and movements are ballistic, recent experiments conducted in this laboratory indicate that forces and movements acquiring the target within 200 ms can be substantially modified by visual input. Three visual control mechanisms were studied: triggering, amplitude control, and error correction. Movements and force responses can be triggered as soon as 150 ms after the presentation of a visual cue. The amplitude of force or movement response can be adjusted within 10–150 ms after response onset. Errors in trajectory can be modified as early as 160 ms after response onset. The results of one experiment demonstrate the speed and accuracy of visual control in targeted motor responses. Step changes in elbow torque were produced in response to a visual stimulus, which cued subjects when to initiate the responses as well how much torque to produce. Visual feedback of the torque responses was provided in selected trials. The order of trials was randomized with respect to what torque was required and whether visual feedback was provided. The analysis of data centered on how two relationships varied over the course of torque responses: 1) the influence of target torque on response torque and 2) the influence of error on subsequent changes in torque. The development of these two influences was compared for torque responses produced with and without visual feedback.

Kinesthetic Control of Targeted Forces and Movements of the Human Arm

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Although kinesthetic input is rapidly conducted to the brain and reaches consciousness, little is known about how kinesthesis controls targeted forces and movements
beyond the reflexive control of muscle length or stiffness. Recent experiments conducted in this laboratory demonstrate several different ways that kinesthetic input can control targeted forces and movements. Three kinesthetic control mechanisms were studied: triggering, amplitude control, and error correction. Although it is well known that motor responses can be triggered by external kinesthetic stimuli, kinesthetic input from an ongoing joint rotation can also trigger (i.e., time the onset of) a subsequent joint rotation during a movement sequence. The amplitude of targeted forces or movements can be adjusted shortly after response onset by kinesthetically cued target information. Velocity errors can also be corrected as quickly as 120 ms after response onset. The results of two experiments demonstrate the speed and accuracy of kinesthetic control of target forces and movements. In one experiment, amplitude control was demonstrated with a bimanual torque matching task, in which the torque target was presented kinesthetically (and visually for the sake of comparison). In another experiment, triggering and error correction were demonstrated during a movement sequence of the elbow and hand. Kinesthetic input from the elbow was found to control the timing of the hand movement with a latency range of 150–1600 ms. Corrective action for velocity errors was initiated within 120 ms after the onset of elbow movement. These results suggest that kinesthetic input plays an active role in target acquisition during force changes and changes in movements.

Is There a Dedicated Processor for Time-to-Contact Judgments?

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Lee (1976) has proposed that actions are able to be time-locked to environmental events because the actor or observer can monitor directly from the optic flow field a single critical variable. This variable, \( \tau \), which is given as the inverse of the relative rate of retinal expansion, has been shown mathematically reliably and unambiguously to specify the time remaining before an approaching object reaches an observer. Two experiments were conducted to determine if access to an expanding retinal image is indeed predictive of the performance of subjects on a simple coincidence-timing task where the approaching motion is of uniform velocity and no spatial uncertainty exists regarding the direction of the approaching motion. In the first experiment 18 subjects viewed either monocularly or binocularly approaching motion generated from a Bassin coincidence-timer in order to test the assumption that timing based on \( \tau \) is equally accessible to one eye as to two. In support of the direct perception notion similar absolute (AE) and variable (VE) errors in timing were observed under both viewing conditions, although some minor differences in bias in terms of early and late responding were found on the constant error (CE) measure. In the second experiment 30 subjects made binocular coincidence-timing judgments from viewing positions either front-on or side-on to the approaching motion. AE, VE and, to a lesser extent, CE were all lower under the front-on viewing condition—this being the only condition in which a true expanding retinal image was available. Conditional support is advanced for the presence of an evolved dedicated processor for time-to-contact judgments based on the direct perception of \( \tau \).
Mechanical Modelling of Motor Skill

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The ability to interpret the underlying processes of motor control and skill acquisition depends largely on both intended and unintended application of biomechanical and kinesiological principles. A movement is perceived in terms of kinetics (forces) and kinematics (displacement and its time derivatives). Also, we can represent a complete movement as a trajectory in space and time. Error information and the resultant feedback relies on a performance criterion or performance model with which the movement can be compared. It is possible both experimentally to determine the performance model by establishing the correct biomechanical principles of the task and with appropriate technology, to enable simultaneous presentation of both the criterion variable and the model. It is therefore reasoned that provision of mechanical principles would assist both the learner and the teacher in gaining insight and mastery of a given gross motor skill.

Modelling Memory in Rats: Enrichment, Social Isolation, and Aggleton’s Object Recognition Task

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Many currently popular procedures to investigate mnemonic processes in rats sample their excellent abilities to solve spatial problems. While spatial tasks represent a rich source to test animal models of human mnemonic disorders, experimental procedures with human and primate subjects often involve nonspatial tasks and object recognition. To foster more direct cross-species comparisons, Aggleton (1985) devised a nonspatial one-trial object recognition test in which rats were rewarded for selecting the novel of two goal boxes in a Y-maze. The present study used Aggleton’s procedures and confirmed the hypothesis that adult rats reared since weaning in an enriched environment, as compared with socially-isolated rats, showed faster learning of his nonmatching-to-sample task. However, the task proved to be more difficult than previously reported, with 8/9 enriched rats and only 2/9 isolated rats reaching criterion performance before a maximum of 650 trials. Rats that achieved criterion were additionally tested, in a counterbalanced order, with a block of five No-delay sessions (i.e., 50 trials), five 60s intertrial-interval (ITI) Delay sessions, and five sessions of 60s ITI + Interference during the delay period: performance declined across these three conditions, respectively. This study shows (i) that object recognition memory is impaired by postweaning isolation; (ii) that interference effects are attainable in Aggleton’s task; but (iii) the suitability of this task requires further validation across different strains and conditions.
The Effect of a Special Enrichment Procedure on Learning and Hippocampal Structure in the Aging Rat

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An environmental enrichment procedure designed specifically to stimulate functioning of the hippocampus was assessed in comparison to an impoverished, (isolated) environment and a standard laboratory (social) environment, for rats aged 9 months and 18 months of age. The enrichment involved 70 days exposure to changing spatial locations of goal items (food and water, toys, running wheel, sleeping box); successive visual discrimination reversals; and negotiation of Lashley type mazes to enter goal areas. The 9 months old enriched rats were significantly more likely to initiate exploration of a novel environment than the other groups, and isolated rats were more exploratory than social controls. Enriched rats learned a radial maze task significantly faster than did the other groups; and on reversal of the radial task, isolated rats made more errors than the other group. These effects were still evident, but diminished, in the 18 month old rats. On structural measures of hippocampal activity, enriched rats had higher synaptic surface densities compared with controls in the outer and middle molecular layer of the dentate gyrus; and higher volume densities of mitochondria in the inner molecular and polymorphic layers of the dentate gyrus.

Reward as Fulfillment of Motor Intentions: A Unifying Concept for the Function of the Mammalian Striatum

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In humans the striatum is regarded as controlling the initiation of motor movements (implicitly ones that have been learned). In experimental animals, a different case can be made, especially from the self-stimulation literature, that the striatum is involved in reward-mediated learning, with the dopaminergic innervation to the striatum serving as the reward signal. These two views of striatal function can be reconciled if the broad concept of 'reward' is divided into two analogous forms: Visceral reward is the fulfillment of innate goals (e.g., obtaining food and drink). Reward as control is the fulfillment of an acquired goal when a sequence of motor acts fulfills a non-visceral intention. Afferents to the midbrain dopaminergic neurons (having a net inhibitory sign) come from the prefrontal cortex via synapses in the 'striosomes' of the striatum. Neurons in the prefrontal cortex represent sequences of events lasting many seconds. These neurons are likely to be influenced by the consequences of responses.
If a response takes place whose consequences silence the activity in a proportion of prefrontal neurons, this releases reward neurons from inhibition, leading to reinforcement of the response. Reinforcement would thus be acquired which produces predictable consequences, regardless of innate motives. This function is envisaged to operate in play activity, and other instances of acquisition of control during which prefrontal cortical neurones come to represent unfulfilled intentions.

Synaptic Modification in the Striatum: A Model

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In the striatal matrix, cortical and nigral afferents converge upon spiny projection neurons, providing a potential site for interaction between stimulus-response connections and dopamine pathways putatively mediating reward. If operant conditioning involves strengthening the corticostriatal synapses, we expect brain stimulation reward to have similar effects. Intriguing observations by Olds (Electroencephalography & Clinical Neurophysiology, 1963, Supplement 24, 219-234) of single unit operant conditioning (SUOC) in the striatum appear to support this. Moreover, Hirata et al., (Brain Research, 1984, 321, 1-8) showed that excitatory input from sensory motor cortex to striatum was modified by stimulation of the substantia nigra. However, their results suggest synaptic attenuation is seen more often than strengthening. This paradox at unit level may be reconciled at network level, if strengthening occurs only at synapses on a selected subset of projection neurons. Since these are mutually inhibitory, a net attenuation of responses of other (nonselected) neurons follows intuitively. This also has implications for changes in the shape of the peristimulus time histogram (PSTH) after dopaminergic activation. We describe a common model for synaptic modification with which both SUOC and dopamine effects on PSTH shape can be simulated. In the model, sufficient coactivation of convergent afferents brings about elevated calcium levels ([Ca$^{++}$]) in depolarized dendritic spines, via voltage-sensitive calcium channels. Dopamine promotes strengthening in only those spines with raised [Ca$^{++}$]. Possible mechanisms are considered, and a computer simulation described.

The Role of NMDA Receptors in the Kindling Model of Epilepsy

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To investigate the role of N-methyl-D-aspartate (NMDA) systems in kindling, the effects of systemic administration of MK-801, a novel noncompetitive antagonist of NMDA receptors, were examined in kindled rats. The results were: (i) Both the seizure stage and afterdischarge (AD) duration of previously kindled seizures from the amygdala were potently suppressed following MK-801 injection (1-4 mg/kg) in a
dose-dependent manner. The maximum effects were observed between 2 and 4 hours after the injection. (ii) The MK-801 also produced significant anticonvulsant actions on kindled seizures from the frontal cortex and the dorsal and ventral hippocampus. The efficacy, however, differed between these kindled sites. (iii) Daily treatment of MK-801 (0.25 and 1 mg/kg) prior to each electrical stimulation of the amygdala significantly retarded kindling seizure development. During drug sessions of 1 mg/kg MK-801 for 19 days, all rats showed only partial seizures and the growth of ADs was strongly prevented. (iv) Pretreatment with reserpine (2.5 mg/kg), a catecholamine depleting agent, did not antagonize the effects of MK-801 on amygdala kindled seizures, suggesting that the effects may not be mediated via catecholaminergic systems. These results indicate that MK-801 has potent anticonvulsant actions on kindled seizures from both limbic and cortical foci, and that NMDA systems may play a critical role in the seizure-triggering mechanism of kindling.

**Modification of Amygdala Kindling by Intracerebroventricularly Administered Gangliosides in Rats**

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Gangliosides, glycosphingolipids which contain sialic acids, are highly concentrated in the central nervous system (CNS), particularly, in the synaptic membrane. Recently, various functions of gangliosides in the CNS have been investigated. The present study evaluated the effects of intracerebroventricularly (ICV) administered total brain gangliosides on amygdala (AM) kindling in rats. The results obtained were: (i) Exogenously injected gangliosides (0.4 and 0.8 mg/4 μl) significantly decreased the afterdischarge threshold (ADT) in a dose-dependent manner; (ii) both 0.8 mg and 0.25 mg gangliosides significantly facilitated AM kindling seizure development by repeated AM stimulation (200 μA, 1 s, sine wave) at 2 hour intervals in a dose-dependent manner, especially, in the late stage of kindling (stage 3–5); (iii) 0.25 mg gangliosides did not affect previously kindled seizures; (iv) 0.8 mg gangliosides had a proconvulsant action in both nonkindled and kindled rats. Epileptiform responses to the gangliosides markedly increased during kindling. In fully kindled rats, generalized clonic seizures with long epileptiform discharges were induced by ICV injection of the gangliosides, and these increased responses lasted for at least 5 weeks after kindling. From these results, it is concluded that gangliosides in the neuronal membrane may play an important hyperexcitable role in the kindled permanent epileptogenesis.
Seizure-Induced Changes in Cerebral Glucose Content, Phosphorylation Rate, and Glucose Utilization

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Delivery of pentylenetetrazole (PTZ, 0.75 mg/kg) via an external carotid arterial cannula induces seizures in rats which have been demonstrated in EEGs (in electrode-implanted animals) to last approximately 30 min. Cerebral blood flow (CBF) rates, measured in these animals using the artificial organ method (Van Uitert & Levy, 1978, Stroke, 9, 67), indicate the convulsant's effect is localized to the PTZ-ipsilateral, rather than contralateral (CL) forebrain. Hippocampal CBF was 1.37 ± 0.34 ml/min-gm (M ± SD) in controls; at 15-min, PTZ = 1.52 ± 0.54 vs CL = 1.19 ± 0.40; at 30-min PTZ = 1.43 ± 0.39 vs CL = 1.11 ± 0.33; at 60-min PTZ = 1.63 ± 0.47 vs CL = 1.31 ± 0.54; and at 120-min PTZ = 1.79 ± 0.56 vs CL = 1.55 ± 0.52. Increased CBF persists, therefore, postictally. Cerebral glucose utilization rates (CMR-glucose) have been measured in seizure states by following the trapping of 2-deoxyglucose analogues over a 15-30-min period either autoradiographically, or with Positron Emission Tomography. The carotid-injection, microwave fixation technique (Oldendorf et al., 1982, Journal of Neurochemistry, 38, 1413) which we employed, utilizes a brief (60-s) experimental time-period, and permits analyses of brain glucose content, glucose phosphorylation rate (K3), and CMR-glucose, before, during, and after seizures. Our data indicate brain glucose concentration (and also brain:plasma glucose levels) are in a constant state of flux ictally and postictally, and recovery is a relatively slow process.

Supported by the Veterans Administration and NIH grant NS22890.

Lasting Changes in Polyphosphoinositide Hydrolysis Coupled with Excitatory Amino Acid-Receptors in Brain Slices of Kindled Rats

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Long-lasting increases in excitatory amino acid-receptor mediated polyphosphoinositide (PPI) hydrolysis in slices of the amygdala/pyriform cortex (AM/PC) of amygdaloid and hippocampal kindled rats was observed. Electrodes were implanted into either the left amygdala (AM) or the left dorsal hippocampus (HIPP). Both groups of the rats were fully kindled and decapitated various days or weeks after the last seizure. PPI hydrolysis was measured by ibotenate (IBO)-stimulated accumulation of [³H]inositol-1-phosphate ([³H]IP₁) in the presence of LiCl. The results were: (i) In the AM-kindled rats, IBO-stimulated accumulation of [³H]IP₁ significantly increased in the AM/PC 24 hours, 1, 2 and 4 weeks after the last seizure. Change in the HIPP was more transient (until 1 week after the last seizure) than in the AM/PC. (ii) Four weeks
after the last seizure, there was a similar magnitude of significant increase in the contralateral (right) and the ipsilateral (left) AM/PC of the AM-kindled rats. (iii) In the HIPP-kindled rats, IBO-stimulated [3H]IP, significantly increased in both the AM/PC and the HIPP 24 hours, 5 days and 15 days after the last seizure. However, 30 days after the last seizure of HIPP-kindled rats, [3H]IP, accumulation significantly increased only in the AM/PC but not in the HIPP. These results suggest that changes in PPI metabolism coupled with excitatory amino acid-receptors in the AM/PC may be associated with the mechanism of development and maintenance of kindled seizures.

Regional Changes of Guanidino Compounds in the Amygdala Kindled Rat Brain

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Many guanidino compounds are widely distributed in mammalian brain tissue. It has been shown that some of these induce epileptic seizures when they are intracisternally administered into the rat brain, and that intrinsic guanidino compounds significantly change in the brain of experimental models of epilepsy, such as chemically- and electrically-induced seizures. In the present study, we investigated regional changes of guanidino compounds in amygdala kindled rats. Electrodes which were inserted into the left amygdala of male Sprague-Dawley (SD) rats were electrically stimulated (200 μA, 1 s, sine wave) once or twice a day until 10 stage 5 seizures appeared. The rats were then divided into 3 groups: sham-operated group without kindling stimulation (N = 7); 24 hours after kindling (N = 7); and 7 days after kindling (N = 6). The brains were removed and divided into 7 regions (cortex, thalamus, left amygdala, left hippocampus, left striatum, right amygdala and right hippocampus), and the levels of 6 guanidino compounds (guanidinoethanosulfonic acid, guanidinoglutaric acid, guanidinoacetic acid, creatinine, arginine and methylguanidine) were measured by fluorometrical analysis. In the right amygdala (non-stimulated side), guanidinoethanosulfonic acid, guanidinoacetic acid (p < .01) and methylguanidine (p < .05) were significantly increased 24 hours after the last stage 5 seizure. In the left hippocampus, guanidinoethanosulfonic acid was increased 7 days after the last seizure (p < .05). These results suggest that amygdala kindling results in significant and lasting change of guanidino compounds, which may be related to the mechanism of kindling in rats.
Excitatory Amino Acids and Adenosine Receptors and Proto-Oncone c-fos in Epileptic, Human, Temporal Gyrus and Hippocampus

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Recent studies in animals suggest that the proconvulsant excitatory amino acids and the anticonvulsant adenosine play important roles in seizure initiation, spread and termination. Furthermore, rodent studies have suggested that the c-fos proto-oncone is in epileptogenesis (Nature, 1987, 329, 441). We are investigating receptors for excitatory amino acids (NMDA, PCP, quisqualate, and kainate) and adenosine (A1 and A2) in cryostat cut (16 micro m) sections of temporal gyrus and hippocampus excised in the routine neurosurgical treatment of intractable temporal lobe epilepsy. We are using the technique of quantitative receptor autoradiography. Preliminary results of these studies will be presented. We have detected, using the technique of immunocytochemistry, for the first time, the presence of c-fos protein in neurons from human temporal gyrus and hippocampus (CA1, CA3 and dentate gyrus) excised from epileptic brain. The distribution of c-fos in human brain matches the distribution of NMDA receptors and follows a pattern similar to that observed in rodent brain. The implications of these studies to understanding the neurochemical abnormalities in epileptic brain will be discussed.

Qualitative Differences In Tactuospatial Motor Learning By Left-handers

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Tactuospatial capacity was studied as a function of subject handedness and hand employed in learning and transfer. Seventy-eight dextral and 75 sinistral blindfolded subjects learned a finger-maze with either dominant or nondominant hand. Transfer
to the untrained hand was assessed with either an identical or a mirror-image version. Left hand acquisition required fewer trials; latencies were shorter using the dominant hand. All dextrals and sinistral subjects using the right hand in acquisition showed superior transfer to the identical maze. Sinistral subjects using the left hand in acquisition demonstrated facilitated transfer to the mirror-image. Results are interpreted as evidence of two qualitatively different hemispheric strategies for encoding tactuospatial information.

Tactile Perceptual Asymmetry: The Influence of Motor Activity and Imagery Instructions

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The purpose of the present study was to examine the degree to which changes in muscular activity modify tactile perception. In two experiments, subjects were presented with a series of pairs of random shapes, one to the fingers of each hand. Their task was to detect the occurrence of a previously learned target shape. Pressing onto the shape was the only movement allowed and other types of motor activity, particularly tracing movements were not permitted. Across experimental conditions subjects were required to change the pressure and hence muscular effort used to press upon the shape. A left-hand advantage was found across all experimental conditions and its size did not change when subjects were required to press either firmly or lightly upon the shapes. This result was also found when subjects were required to apply uneven pressure between the hands. One-half of the subjects also performed the experimental conditions following instructions to use imagery. This produced an enhancement of right-hand performance on the task with a loss of the left-hand advantage, suggesting that observed tactile perceptual asymmetries are easily over-ridden by higher-order processes. It is concluded that the present dichaptic monitoring technique supplies a relatively pure measure of tactile perception free of possible confounding effects arising from higher-order cognitive, motor and memory processes.

Neurophysiological Correlates of Visual and Movement Imagery

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For some time researchers within cognitive psychology have avoided the fundamental issue that images are part of the conscious state. Modern brain imaging techniques
have in some instances only added to this confusion. Recent experiments using Electroencephalographic (EEG) topography of visual imaging in normal subjects suggests that visual images are generated and accessed in a trimodal system (Marks, 1986, Imagery 2, Proceedings of the 2nd International Imagery Conference, 152–258). Marks suggested: a) That there appeared to be an 'image-compiling module' in the right frontal lobe which computed and composed the image from memory. b) A ‘long-term memory file’ containing elements of the visual appearance of objects, located in the occipital and parietal regions. c) An ‘image readout’ in the left temporoparietal area which provided monitoring of the image. This study attempts to clarify these suggestions using a visual and movement imagery paradigm. Twelve normal, righthanded subjects were classed as high or low visual–movement imagers and were included in a EEG topographical mapping experiment under conditions of visual imagery and movement imagery. Preliminary results indicate that, within high imagers, in certain cortical areas, there are significant differences from baseline to imagery situation, for both visual and movement conditions. This is not apparent in the low imagers. Results also indicate a marked laterality, within the high image movement condition, in favour of the left side.

Impaired Visuospatial Functions in Two Adults With Left Hemispherectomies and Intact Language Abilities

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Patients who sustain extensive damage to the left ‘speech’ hemisphere early in life may demonstrate recovery of language functions. In patients who have had left hemispherectomies, language functions must be mediated entirely by the right hemisphere. Visuospatial functions and prosody, normally mediated predominantly by the right hemisphere, have not previously been studied in these cases. One possibility is that the isolated right hemisphere mediates all functions normally mediated by the whole brain, and another possibility is that visuospatial functions and prosody are disadvantaged as a result of the right hemisphere’s involvement in language. Neuropsychological assessments were carried out on two adults aged 45 and 34 years, many years following the surgical removal of their left hemispheres to treat intractable epilepsy. The subjects had left-hemispheric damage from infancy, although their hemispherectomies were not performed until they were aged 17 and 18 years old. When assessed, both subjects had WAIS-R Verbal and Performance IQs in the Borderline to Average range, had been fully employed for many years, and lived independently. Their verbal functions were remarkably intact, but they demonstrated moderate to severe impairment on the copy and recall of the Rey Complex Figure, Locomotor Mazes, mental rotation tasks, nonverbal imagery tasks, Mooney’s Closure Faces test, and various drawing tests. Their performances on tests of prosody were normal. The implications these findings have for theories of the development of hemispheric specialization will be discussed.
Electrical Brain Potentials Elicited in Response to Discrete Stimuli in Patients with Alzheimer's Disease

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Objective biological markers of mild Alzheimer's disease are needed, especially since the incidence of this disorder is increasing. Research from our laboratory suggests that an abnormal delay in the latency of the P300 component of evoked response potentials (ERPs) identifies with a high degree of sensitivity and specificity patients with a moderate to severe dementing process, but not those in the early stages of Alzheimer's disease. These findings are based on analyses of the average evoked potential obtained via many repetitions of a particular type of stimulus. Average ERP waveforms, however, provide limited if any information regarding the brain's response to a specific (individual) stimulus. An analysis of single-trial waveforms may provide meaningful information with regard to 'real-time' cognitive processes elicited by individual stimuli. Such analyses may be particularly useful in uncovering the reason why certain Alzheimer patients have no identifiable P300 component: is this due to artifact, or to a marked disturbance of those cognitive processes reflected in the P300 component? At present, these patients are being excluded from P300 analyses. We are examining the possibility that the absence of a P300 component is itself an indicator of disturbed cognition, and thus, whether it provides information useful to the diagnosis of the early stages of Alzheimer's disease.

Linguistic Deficits Following Treatment of Posterior Cranial Fossa Tumors in Children

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Although posterior fossa tumors account for over half of all pediatric intracranial neoplasms (Segall, et al. 1985, Cancer, 56, 1748–1755) little information is available in the literature on the speech–language abilities of children who have undergone treatment of such tumors (Rekate, et al. Archives of Neurology, 42, 697–698). In the present study, ten children aged between 6 and 16 years who had undergone surgery for the removal of a posterior fossa tumor were assessed at least one year postoperatively to determine the incidence and severity of any associated speech or language deficits. Eight males and two females were included in the sample. The subjects were administered a battery of speech–language tests including: language screening, articulation, dysarthria assessment and perceptual speech analysis. The results indicated that dysarthria and/or language impairment occurred in some cases subsequent to surgical removal of posterior fossa tumors. The occurrence of muteness immediately postsurgery would appear to indicate a poor prognosis of speech abilities. A possible link between the occurrence of long term language disabilities in these children and postsurgical radiotherapy is documented.
Aphasia Following Thalamic and Striatocapsular Lesions of Vascular Origin

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The language abilities of six cases with chronic subcortical brain lesions, centered on either the thalamus or basal ganglia, were investigated. The results of standardized language assessment indicated that longlasting, atypical, fluent aphasia was present in all subjects. Considerable variation existed between the language abilities of each subject assessed and a single, invariable 'subcortical aphasia' syndrome was not evident. In no case was the language disturbance able to be classified into one of the traditional cortical aphasia syndromes. The language assessment results were used to evaluate a model of the role of the subcortical structures in language proposed (Crosson, Brain and Language, 1985, 25, 257-292). Crosson's model is based on the assumption that preverbal semantic monitoring is subserved by the subcortical structures. Although the six subjects had deficits in the semantic level of language, the presence of other aphasic characteristics (example; agrammatism, verbal dyspraxia, and auditory comprehension deficits), and the lack of evidence to support the existence of preverbal semantic monitoring, indicated that Crosson's model may be inadequate to describe the role of various subcortical structures in language.

Neuropsychological Applications to Corporate Business Management: Superficial Analogies or Substantive Possibilities?

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Well-established precedents now exist for the application of psychodynamic principles, personality testing, and social psychological research findings to corporate business management problems of personnel selection and evaluation, employee motivation, leadership training, organizational development, and marketing. There are now significant new trends suggestive of an attempt to add to the business management expert's armamentarium, arguments based on evidence drawn from early findings in the neurosciences, particularly neuropsychology. Strongest among these current trends seems to be the incorporation of neuropsychological findings about hemispheric specialization into arguments bolstering one or another perspective on employee motivation, leadership training, and market strategy. Programmes loosely described as intending to free right-brain function from left-brain dominance to promote employee creativity and leadership are being utilized by major corporations. Within the area of marketing research, which includes product design, packaging, and advertising promotion, neuroscientific research strategies of brain wave mapping have been applied to problems of predicting consumer response to varied product presentations. There are no definitive controls preventing the appropriation of psychological knowledge by nonpsychologists to other fields of specialization. This may well be a desirable state of affairs through which psychological knowledge has become more widely disseminated and the horizons of psychology raised. But, can such as easy conclusion of benignity be drawn when still often tentative neuropsychological findings are appropriated to serve corporate goals without the specific monitoring of the neuropsychologist?
Ego Defenses in Anxiety Disorders

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The Defense Style Questionnaire was relabeled in terms of DSMIII defenses and administered to three groups: normal population, family practice patients, and patients with anxiety disorders. The preferred factor structure identified mature defenses (sublimation, humor, anticipation, suppression), neurotic defenses (undoing, altruism, idealization, reaction formation), and immature defenses (projection, passive aggression, acting out, etc). Factor scores varied systematically with group membership and with measures of total symptoms. In this cross sectional study, the vulnerability factors of neuroticism, locus of control and defensive style were all correlated with neurotic symptoms, but defense style added little to the variance explained by the other two. Within the patient group however, neuroticism and locus of control did not differentiate between panic disorder, agoraphobia, social phobia and obsessive compulsive disorder, while defensive style showed patterns characteristic of each disorder.

The Rise and Fall of the Benzodiazepines: A Cautionary Tale

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Chlordiazepoxide, synthesized in 1957, heralded the arrival of the benzodiazepine group of drugs. Early publications supported their efficacy in the treatment of anxiety and in particular emphasized their safety in use. Problems with dependence, withdrawal, impaired psychomotor performance, anterograde amnesia and disinhibition were not well recognized for two decades. This would not surprise if these drugs were little used but through the 60's and 70's they were best sellers and Valium was known to all. In January 1988 the British Committee on Safety of Medicines published a strongly worded statement about the current indications which, in their opinion, are few. Doctors now face the possibility of litigation from patients as a consequence of prescribing these drugs. An attempt is made to understand this historical sequence with reference to the characteristics of the drugs themselves, the needs of patients and doctors, the drug industry, the sociocultural climate of the times, and the increasing need for informed consent and accountability.

Modifying Effects of Trait Anxiety and Depression on 5-HT Induced Changes of Behavior in Healthy Subjects

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The present paper is based on two observations: 1) Decreased 5-HT brain levels and receptor hypersensitivity have been reported to be characteristic of depression and
anxiety (e.g., Hendrie et al., 1987, 29-46); 2) Decreases in 5-HT transmission are associated with an increase in performance and a decrease in behavioral suppression (e.g., Soubrie, Behavioral and Brain Science, 1986, 9, 319-364.). So far, little is known about how performance and behavior are affected by 5-HT uptake inhibitors in subjects of different initial levels of 5-HT activity possibly based on differences in anxiety and depression. Therefore, the present investigation was designed to answer the following questions: Will subjects selected according to high and low scores of anxiety and depression differ; 1) with respect to emotional states of anxiety, 2) with respect to indicators of performance and activity. In a double blind balanced crossover design 60 mg of the 5-HT uptake inhibitor fluoxetine and placebo were administered to 24 healthy male volunteers divided into high and low groups according to questionnaire scores of trait anxiety, experience of stress, and neurotic depression. All subjects were tested by choice reaction time and scales of activity and state anxiety. Analyses of covariance using baselines as covariates and analyses of variance of change scores revealed significant interactions between neurotic depression and drug for choice reaction time as well as between experience of stress and drug for self-rated feelings of energy. Fluoxetine decreased feelings of energy and performance in stressed and neurotic subjects. Feelings of state anxiety did not seem to be affected by the substance, nor did trait anxiety modify drug effects.

MR/Har and MNRA/Har Maudsley Rat Strains: Variation in Anxiolytic Drug Effects in an Animal Model of Anxiety

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Two strains of Maudsley rats have been selectively bred for open field (OF) defecation. The Maudsley Reactive strain (MR) exhibits high levels of OF defecation while the Nonreactive (MNRA) strain exhibits low levels of OF defecation. This difference in OF behavior has been interpreted as an indicator of 'emotionality' and as providing an animal model for studies of anxiety. MR and MNRA rats which showed differences in OF defecation also showed marked differences in a Conditioned Suppression of Drinking (CSD) paradigm, in which animals were trained to drink from a tube which was occasionally electrified (0.5 mA) signalled by a tone. NMRA rats accepted significantly more shocks than MR rats. Punished responding and strain differences were increased substantially by diazepam and by pentobarbital, modestly by buspirone, and not at all by propranolol. Effects of anxiolytic drugs appear to be specific to both the drug and the genotype.
Drugs, Anxiety and the Brain: not by the BIS Alone

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Gray's neuropsychological theory of anxiety and criticisms of it are briefly reviewed, as are the results of studies by the authors examining the effects of three different classes of anxiolytic drug on the contingent negative variation (CNV) recorded while subjects performed a Go/NoGo avoidance task which includes both active and passive avoidance: (i) Nicotine (cigarette smoking); (ii) Barbiturate (Sodium Amytal) and (iii) Benzodiazepine (Midazolam). These drugs were found to consistently affect the Go CNV (evoked in the 'Go' or active avoidance condition) which reflects changes in subjective stress, but no consistent effect was found in the NoGo CNV (evoked in the ‘NoGo’ or passive avoidance condition) which reflects changes in subjective arousal. It is suggested that: 1) At the human level, trait anxiety reflects a predominance of a lateralized (left hemisphere) cortical ‘activation’ process involved in motor readiness; 2) This cortical process underlies a critical cognitive aspect of human anxiety, namely ‘worry’; 3) This cortical process may represent a cortical extension, at the human level, of Gray's septohippocampal system; and 4) The anxiolytic properties of antianxiety drugs may be mediated in people through effects on these cortical mechanisms. Finally, it is shown how this analysis may help to resolve some paradoxes in Gray's theory.

Multiple Neuronal Processes Contributing to Anxiety

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In the clinic, anxiety, or its elaboration, is affected in a similar manner by drugs of widely different chemical types. These 'anxiolytic' drugs also have surprisingly similar behavioral profiles in animal tests. It is tempting, therefore, to view anxiety and anxiolytic action in terms of a unitary psychological–neural process. Hippocampal rhythmical slow activity can be driven by electrical stimulation of the septum. All anxiolytic drugs so far tested were found to have a similar effect to each other in this test—an effect which was reproduced by depletion of hippocampal noradrenaline or by facilitation of GABA. However, depletion of noradrenaline only reproduces a part of the behavioral profile of the anxiolytic drugs. Hippocampal rhythmical slow activity can also be elicited by electrical stimulation of the reticular formation. This test is neurophysiologically distinct from septal driving. All anxiolytic drugs so far tested were found to have a similar effect to each other on this test—including buspirone, which does not interact with GABA. Depletion of noradrenaline had no effect. These results suggest that anxiolytics have at least two neurally and pharmacologically separate actions within the septohippocampal system, both of which can contribute to their behavioral profile. These and other data suggest that anxiety, or its behavioral elaboration, involves multiple independent processes.
Down Syndrome: Initiation of Discrete, Rapid Movements

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Both an inability to form neuromotor programmes and hypokinesis are thought to contribute to diminished and/or slow movement which is often characteristic of individuals with Down Syndrome (DS). Thus DS subjects would be expected to exhibit longer reaction times (RT) to more complex movements. If the deficit is strictly related to programming the premotor time (PMT) component would increase while hypokinesis would more likely influence the peripheral motor time (MOT) component of RT. Three levels of movement complexity were employed; pointing (P), hitting one target (T1) and hitting two targets in succession (T2). All movements began from an identical starting position. Myoelectric data were recorded (EMG) from anterior deltoid, biceps, brachioradialis and index finger extensor muscles. Data from control subjects revealed little difference in RT among the three movement complexity conditions. PMT was not different across conditions but was shorter to proximal muscles. Data from DS subjects revealed longer RTs than controls and considerably longer RTs to T2 compared to the T1 condition. In addition, PMTs for DS subjects tended to be shorter to peripheral muscles and more variable than for control subjects. Analyses of the EMG profiles indicated that the patterns of activity for DS and control subjects were different with a step-like onset observed in controls and a ramp-like onset observed in DS individuals. One possible explanation is that the ‘strength’ of the neuromotor signal is weaker in DS individuals resulting in slower onset of, and rate of, muscle contraction with correspondingly longer RT.

Sensory-Motor Function Profiles Following Acute Brain Damage via Single-Case Graphical Analysis Techniques

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A graphical analysis procedure has been developed to improve the interpretation of serial sensory-motor (S-M) function data from individual subjects following acute brain damage. The analysis has been applied to 11 stroke patients assessed longitudinally over 12 months on a computerized S-M test battery. Except for grip strength, the primary measures studied were all of proximal arm function: strength, reaction time,
speed, steadiness, steady movement, and an aggregate of preview-random, step, and combination tracking. Evaluation of the results showed that five graphs are necessary to demonstrate fully neurological impairment and recovery of any particular S-M function: Performance, Record (i.e., best performance), Record Increment, Differential of Records, and Differential of Record Increments. Record graphs can give better separation than Performance graphs of patient and normal data, or between arms in the same individual. Differential graphs can sometimes indicate impairment and/or recovery in the affected arm not evident in absolute (i.e., performance, record, record increment) graphs. Absolute, but not differential, graphs can show impairment and/or recovery in the asymptomatic arm. Overall, serial graphic analysis of single cases allowed display of individual profiles but unequivocal impairment and recovery could not be as easily demonstrated as for group analysis.

Sensorimotor Integration Capacity of Stutterers and Nonstutterers

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Stuttering is a disorder of speech motor control. Among hypotheses concerning its specific nature, deficiency in sensorimotor integration processes has been a recurring theme. Some have proposed anomalous lateralization of such processes. Others, noting the similarity between stuttered speech and disfluency induced in nonstutterers by delayed auditory feedback, have argued that incorrect or inadequate sensorimotor integration leads to control system breakdown. This presentation concerns a replication and extension of a previous study in which we addressed these issues. Both studies used transfer function performance measures of stutterers and nonstutterers engaged in auditory and visual pursuit tracking. Auditory performance using left-eared versus right-eared stimuli was compared across groups, as was auditory versus visual performance. Neither study supported the laterality hypothesis, but in overall performance stutterers were inferior to nonstutterers on auditory tasks but comparable on visual tasks. Stimulus-response phase lag provided the key measure supporting the hypothesis of control system breakdown. The first study showed this effect strongly, but it was less striking in the second. This could be attributable to sampling but we believe an intentional methodological difference between the studies is responsible. Extensive practice was given prior to testing in our first study but was minimal in the second. We interpret the observed difference in comparative performance in the two practice conditions as offering new information about the sensorimotor integration capacity of stutterers.

Is Motor Planning Impaired in Parkinson's Disease?

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There is debate in the literature as to whether ability to form and execute motor plans is affected in Parkinson's disease. We have studied the performance of 16 patients with
Parkinson's disease, both on and off drugs, and 16 age and sex matched control subjects on a range of computerized tracking tasks (preview and nonpreview forms of sine, random, and step inputs, plus a random-step combination) and related tests. All subjects were right handed and only the right arm was tested using a steering wheel to measure motor output. Order effects were controlled for by a randomized cross-over design. Patients with Parkinson's disease performed worse on all 7 forms of tracking. However, on nonpreview tracking they were not disproportionately worse than the controls on the sine relative to the random input. When given a preview of the random input, patients showed an improvement in performance which was less than that of controls (16% vs. 26% $p < .05$). This indicates that patients with Parkinson's disease are not significantly affected in their ability to employ a simple predictive motor strategy based upon recognizing, memorizing and utilizing the repetitive nature of the sine target signal. However, their ability to carry out more complex motor planning involving integration of visual input with motor response seems defective. Patients' visuospatial perception for elements of the task was reduced ($p < .01$) and it is uncertain to what extent this affects motor planning.

**CT Scanning in Cervical Disc Herniation**

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Water soluble myelography and postmyelographic CT scanning are the usual imaging procedures for the preoperative assessment of cervical nerve root compression syndromes. For the last four years we have performed high resolution CT without intravenous or intrathecal contrast media in more than two hundred such patients. More than fifty of these patients have had surgery. The surgical findings are compared with those of the CT scans and with other investigations (when performed). As a result of this study it may be concluded that non contrast CT scanning may be the only imaging procedure needed for the investigation of cervical radiculopathy. As is the case with lumbar spine CT, when the plain CT scan does not answer the clinical question, myelography and other studies may be necessary.

**Otolith Function and Roll-Tilt Perception**

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While rotating on a fixed chair centrifuge in an otherwise darkened laboratory, participants were required to indicate their perception of the direction of the resultant gravitoinertial force by setting to the horizontal a small motor-driven illuminated bar which was attached to the chair but could be rotated in the subject's frontoparallel plane. Normal subjects accurately align this bar with respect to the resultant force which (in the dark) they assume to be the gravitational vertical. This percept is called the oculogravic illusion. Patients after bilateral vestibular neurectomy do not sense...
the resultant force accurately implying that roll-tilt perception mainly depends upon vestibular (otolithic) function. Patients who have undergone a unilateral vestibular neurectomy one week prior to testing show a marked asymmetry in roll-tilt perception. Even at rest they set the bar down on the side of the operated ear for it to appear to be gravitationally horizontal. With increasing angles of the resultant force they show an increasing interaural difference in roll-tilt sensitivity due mainly to a decreased sensitivity for resultant forces directly towards the operated ear. Over the next 6 months there is a progressive decrease in both the error in the baseline settings and the interaural difference in roll tilt sensitivity. These results appear to be a manifestation of otolithic compensation. The altered baseline settings are probably due to a tonic change in eye torsion resulting from the unilateral vestibular neurectomy.

Gaze Instability Following Unilateral Labyrinthectomy

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Using scleral search coils we have shown that patients have continuing deficiency of the vestibulo-ocular reflex (VOR) toward the lesioned side up to one year after unilateral labyrinthectomy. Previous reports have indicated no reduction in VOR following labyrinthectomy, but these studies were done using low velocity rotational tests which probably allow the subject to use non vestibular mechanisms to stabilize gaze. Subjects sat in darkness wearing a head-fixed coil and a scleral contact lens coil. Head and gaze velocity were measured to within 3 deg/s and sampled at 600 Hz. A fixation light at 1.0 m was extinguished and the subject's head moved passively at up to 250 deg/s horizontally or vertically. Two indices of labyrinthine function were calculated - head vs gaze velocities and VOR gain (Eye/Head). Data from two patients who have had bilateral labyrinthine sections indicate that nonvestibular reflex eye movements occur after the first 100 ms of a head movement. Accordingly only velocities up to the peak of head velocity were used. Results show that in 37 normal subjects, gaze velocities up to 25 deg/s occurred during head movement both vertically and horizontally. In 5 patients with normal preoperative VOR, gaze stability fell following unilateral labyrinthectomy. Stability did not recover when measured at varying times up to one year. On the intact side a drop in gaze stability which was followed by recovery was sometimes seen.

MK801, a Potent NMDA Receptor Antagonist, Disrupts Plasticity Following Inner Ear Lesions in the Guinea Pig

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Surgical removal of the receptors in one inner ear results in high frequency reflexive eye movements called spontaneous nystagmus, as well as a roll-tilt of the head and
body toward the lesioned side due to the collapse of postural reflexes. These symptoms are similar in all mammalian species. Although the vestibular receptors do not regenerate once removed, many ocular motor and postural symptoms disappear over 2–3 days, in a process of behavioral recovery known as vestibular compensation. Because there is no peripheral recovery, vestibular compensation must be a result of CNS plasticity. Single neuron recording has shown that approximately normal electrical activity returns to ipsilateral vestibular nucleus neurons in the brainstem despite the absence of peripheral vestibular input. The mechanism of this neural recovery is unknown, however alterations in the neurotransmitter receptor activation of deaf-ferented vestibular nucleus neurons have been suggested. Since the N-methyl-D-aspartate (NMDA) receptor has been implicated in other examples of CNS plasticity, we have investigated the effect of the potent non competitive NMDA receptor antagonist MK801, on the maintenance of vestibular compensation. Guinea pigs received a surgical unilateral labyrinthectomy, and following compensation, were given 0.5 mg/kg i.p. injections of MK801. Such injections resulted in a reappearance of spontaneous nystagmus to a level which was approximately 50% of the maximum observed following labyrinthectomy. Saline injections in the same animals had no effect on compensation. MK801 injections caused no nystagmus in normal animals. These results suggest the possibility that the NMDA receptor may contribute to the neural changes responsible for vestibular compensation.

Suggested Roles for the Cerebellum in the Regulation of the Gain of the Vestibulo-Ocular Reflex

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It has been known for a considerable period that changes in the visual environment, produced, for example, by magnifying lenses, lead to long-term changes in the gain (i.e., the amount of eye movement generated in response to a given head movement) of the vestibulo-ocular reflex (VOR). The discovery that lesions of the cerebellum, in particular of the flocculonodular lobe, abolished or very much reduced these changes in gain, together with the demonstration of mechanisms that could produce long-term alterations in the operations of the cerebellar cortex, led to the suggestion that changes in VOR gain were generated and maintained by these cerebellar mechanisms alone. More recent experimental work, while it has confirmed that changes in VOR gain cannot occur without an intact cerebellum, has suggested that changes are a result of processes occurring in brainstem nuclei that are involved in the transmission of vestibular information to the motor nuclei that operate the extrinsic eye muscles. A comparison of the experimental results obtained in a number of studies with theoretical work has indicated that both the cerebellum and brainstem nuclei may be involved, with the cerebellum being responsible for the relatively early phases of gain alteration with changes in the effectiveness of synapses in the brainstem nuclei accounting for long-term alterations in gain. The theoretical and practical implications of some possible mechanisms for changing VOR gain will be presented.