Functional Neuroanatomy and Neurophysiology

FNN1

DISSOCIATION BETWEEN ATTENTIONAL, MOTIVATIONAL AND SPATIAL COMPONENTS OF EXPLORATION IS UNDERLIED BY DIFFERENT NETWORK OPERATIONS IN LIMBIC AND NEOCORTICAL AREAS OF THE NHE RATS

A. Gallo and A.G. Sadile
Lab. Neurophysiol. Behav. & Neural Networks, II Univ. Naples, Italy.

In order to study the role of non cognitive components, such as motivation, attention and emotionality, in the integration of learning and memory processes, and its neural substrates a neurogenetic approach has been followed in two genetic models, the Naples High Excitability (NHE) and Naples Low Excitability (NLE) rats using behavioral and functional imaging analysis. To this aim, adult male rats of the NHE, NLE and random-bred controls (NRB) were used in separate experiments. *Behavioral analysis:* rats were tested in an 8-arm radial maze (Olton-maze) with extra-maze cues. They were either kept at 80-85 % body weight (Exp. 1) or were fed ad-libitum and were given also two pieces of chocolate per day at about the testing time (Exp. 2). In both experiments, non reinforced maze exploration on day 1 was followed by reinforcements of alley visits during shaping sessions and restriction of baited arms to a single arm. The latter was the same for each rat and differed among rats on consecutive days. The behavior was videotaped and analyzed off-line. The results indicate that (i) there was no difference among the three rat lines in working memory during non reinforced maze exploration, independent of the motivational level, (ii) at high motivational level (Exp. 1) rats of all three lines showed a higher working memory in finding the single baited arm than under low motivational level (Exp. 2), (iii) at low motivational level, both NHE/NLE showed a more stable reference memory than controls, and (iv) NHE rats paid little attention towards reinforcement upon visiting the baited arm. *Functional imaging*_analysis: brains were frozen, sectioned, and stained for quantitative histochemistry of cytochrome oxidase (C.O.) together with standards (brain homogenates) of known C.O. activity. Densitometric measurements converted to C.O. activity units (mmol/min/g wet weight tissue) were carried out across the anterior forebrain. Significant differences were found in medial frontal, entorhinal, and perirhinal cortex, and basolateral amygdala. NHE showed greater C.0. activity than NRB in entorhinal cortex (superficial layers) and lower activities in perirhinal cortex and basolateral amygdala. NLE showed greater C.O. activity than NRB in medial frontal cortex and lower activity in perirhinal cortex (dorsal region). Genetic selection led to greater metabolic capacity in the medial frontal cortex correlated to low behavioral reactivity and in the entorhinal cortex correlated to high behavioral reactivity. Lower metabolism in perirhinal cortex and basolateral amygdala was linked to high behavioral reactivity to spatial novelty. Thus, behavioral and functional neuroimaging analysis suggest that the neural substrates of cognitive and non cognitive components of exploration are underlied by different network operations in the neocortical and limbic cortices in the NHE and NLE rat lines.

Supported by TELETHON Italy Grant E.513

FNN2

REGULAR, IRREGULAR AND BURST FIRING MODES OF SUBSTANTIA NIGRA DOPAMINE CELLS IN THE FREELY MOVING RAT

B.I. Hyland[1,3], J.N. Reynolds[1,3], C.G. Perk[1,3], and R. Miller[2,3]*
[1]Dept. of Physiology; [2]Dept. of Anatomy and Structural Biology; [3]Neuroscience Research Centre
University of Otago, P.O. Box 913, Dunedin, New Zealand

The normal activity patterns of dopamine cells and the determinants of these patterns are of considerable interest, as the midbrain dopamine system is implicated in behavioural reward, movement, drug addiction and schizophrenia. In slices, regular and irregular firing modes are seen, while in anaesthetised preparations bursting activity has been well characterised. In conscious animals, dopamine cells burst in response to behavioural stimuli, but little information is available on the incidence or characteristics of the different firing modes, so it is uncertain to what extent the data from reduced preparations applies to the awake animal. To investigate this, rats had microwire electrodes implanted in the substantia nigra, under general anaesthesia. Subsequent recordings (10 minutes) were obtained using standard electrophysiological procedures with the animal free to move in a perspex box, but performing no task. Fifty nine presumed dopamine cells (inhibited >50% by i.p. apomorphine, action potential >1 ms, firing rate <10 Hz) were analysed, from 7 rats. Of these, 15 (25%) had "regular" spike activity (= 2 obvious autocorrelogram peaks, mean 2.5±0.7). The mean ± 1SD interpeak interval was 252.9 ± 68.1 ms, consistent with the firing rate of the cells (4.0 ± 0.9 Hz). These cells had a low coefficient of variation (CV; 45.7 ± 21.3) and few bursts (0.1 ± 0.2 bursts/s and 8.9±14.2 % spikes in bursts; intra-burst firing rate = 17.8 ± 3.5 Hz; burst onset =an inter-spike interval < 80 ms, burst end = interval > 160ms). The remaining non-regular cells included "irregular" and "bursting" mode cells (burst rates ranging from 0.1 – 75 % spikes in bursts). Overall, the characteristics of these non-regular cells were: firing rate = 3.6 ± 1.7 Hz; CV = 66.0 ± 21.7; spikes in bursts = 25.0 ± 21.3 %; intra-burst firing frequency 21.0 ± 4.7 Hz. To compare the characteristics of these "spontaneous" bursts with those evoked by specific stimuli, we analysed 7 presumed dopamine cells excited by reward delivery during a lever-press task. The intra-burst firing rate for bursts occurring after the reward (31.9±8.57) was significantly higher than for bursts occurring at other times (20.1±2.6 Hz, p=0.01, Student's t-test). These results confirm that regular, irregular and bursting activity modes occur in the conscious rat and that "spontaneous" bursts are similar to those in reduced preparations. The higher intra-burst frequencies seen in response to rewards may reflect specific enhancement of synaptic drive .

Supported by the Otago Medical Research Foundation and New Zealand Neurological Foundation.

FNN3

BRAIN WEIGHT SELECTION IN MICE. BEHAVIOURAL CORRELATIONS

N.V Markina, R.M Salimov, and I.I. Poletaeva*
Biology Department, Moscow State University and Institute of Pharmacology, Russian Academy of Medical Sciences, Moscow, Russia

Heterogeneous mouse population derived from CBA, DBA/2, C57BL/6, C57Br and A/Sn inbred strains was used to initiate the brain weight selection. This selection was based on the relative brain weight scores and was described earlier (Popova *et al.*, 1997). This interstrain difference in the brain weight is now (F19-20) 60-70 mgs, which is about 16-20% of initial population brain weight scores. Body weight differs in 2-4%. Large brain selection mice (LBW) of several generations were significantly more efficient in T-maze learning, less explorative in the open-field test and in closed cross-maze. Small brain weight (SBW) mice had higher immobility scores in Porsolt and tail-fixation as well as slippery funnel (Salimov *et al.*, 1996) tests. SBW were also more inclined to perform the stereotyped locomotion in cross-maze. No significant differences in extrapolation capacity cognitive task were revealed across selection generations, which confirms previous data (Poletaeva *et al.*, 1993). The data on reciprocal hybrids behaviour will be presented. In both LBW and SBW mice the behavioural asymmetry was evident as the tendency to move to the right in t-maze learning and extrapolation tasks. Since such asymmetry was absent in mice of initial population the observed phenomenon could be the consequence of the brain weight selection.

Supported by RFFI N98-04-48440 and MGSE N97-10-266 grants.

FNN4

DIRECT VESTIBULAR CONTROL OF CARDIOVASCULAR REGULATION IN MAN

A. Radtke[1,2], K. Popov[2,3], A. M. Bronstein[2], and M.A. Gresty[2]*
[1]Virchow Klinikum, Humboldt Universität, Berlin, FDR, [2] MRC Human Movement and Balance Unit, National Hospital for Neurology and Neurosurgery, London WC1N 3BG, UK and [3]I I T P, Russian Academy of Sciences, Moscow GSP-4, Russia.

Recent animal studies have shown direct projections from the vestibular system to centres for cardiac and respiratory control (1). We present evidence for the existence of short latency vestibular-autonomic projections in man. The method used to stimulate the vestibular end organ was a small 'drop' of the head[2]; a technique which has proven effective in distinguishing vestibular from non-vestibular responses in skeletal muscle. Subjects lay supine on a bed with their head raised 10cm in a sling which released abruptly (<1ms) causing the head to fall for ≈140ms onto the cushioned surface. Recordings were made of head acceleration, blood pressure (BP) from the radial artery, ECG, finger plethysmography, capnographic respiration. Surface emg from orbiocularis, sternmomastoid, abdominal and intercostal muscles was also monitored. The main experiment was to trigger 'drops' from the ECG R-spike and

compare recordings taken pre- and post-drop. 12 normal subjects were exposed to drops timed 170ms and 570ms after a R-spike (total 16 drops). Their results were compared with those of 9 bilateral labyrinthine defective patients. Control conditions comprised: responses to a 'startle' of 110dB, 1kHz, 500ms duration tone also triggered by the R-spike (total 16) and 8 self released drops which were unsynchronised with the ECG. The order of dispensing drop timing and stimulus conditions was balanced within and across subjects. In a further 3 normal subjects drops were given 170, 370, 470 and 570ms after the R-spike (8 drops at each interval) to establish response latencies with precision. For normal subjects, drops timed 170ms-470ms after a heartbeat significantly shortened the mean RR interval between the immediate pre-drop heartbeat and the 1st beat after the drop. The interval between the 1st and 2nd post-drop beats was also shortened. Drops timed at 570ms only shortened the interval between 1st and 2nd post drop beats. In labyrinthine defective patients drops timed 170 and 570ms after a heartbeat only succeeded in reducing the RR interval between the 1st and 2nd post drop beats. Startling sound did not affect RR intervals in either normal subjects or patients. Self release *increased* the RR interval between the pre- and post-drop heartbeats in all subjects. Systolic BP tended to rise in response to all stimuli in all subjects but only after 2-3 heartbeats. Similarly plethysmographic responses showed peripheral constriction in all subjects for all conditions. The results demonstrate that stimulation of the vestibular organ in normal subjects is responsible the acceleration of heart rate observed at a shortest latency circa 500ms in response to a passive unexpected transient acceleration of the head. Stimulation of other sensory inputs, as with the patients, affected heart rate only after 1-1.5s. One may speculate that the vestibular system has the special function of providing a fast influence on the heart during rapid spatial reorientations.

(1)Yates BJ. (1992) *Brain Res Rev* 17:51.

FNN5

CONTEXT EFFECTS ON PITCH DISCRIMINATION: EVIDENCE FROM ERP RECORDINGS

E. Brattico, M. Tervaniemi, and R. Näätänen*
Cognitive Brain Research Unit, Dept Psychol, Univ Helsinki, Finland

Psychophysical evidence indicates that listeners prefer simple sound relationships to more complex ones. For instance, Cuddy (1971) found that sound sequences with triadic and octave relationships were learned more rapidly than were sound sequences without such relationships. Also Schellenberg and Trehub (1994) showed that the perceptual processing of tones with simple ratio is facilitated compared with tones with a complex ratio. The auditory event-related potentials (ERPs) can reveal the physiological basis of information processing. In particular, the cognitive ERP component called *mismatch negativity* (MMN) may help to characterize the brain mechanisms of auditory sensory memory and involuntary attention. It is typically elicited in an unattended oddball paradigm where a stream of frequently occurring sounds ('standards') is interrupted by an infrequently presented sound ('deviant'), differing from the 'standards' in one or several physical or abstract sound parameters (for a review, see

Näätänen, 1992). A previous MMN study demonstrated that pitch discrimination is facilitated when tones were spectrally rich compared with tones that included only the fundamental frequency (Tervaniemi et al., submitted). The present study aimed at investigating whether pitch discrimination could be influenced at a pre-attentive level also by the context in which the sounds are embedded, and whether the degree of this influence is modulated by musical training. Ten musicians and ten non-musicians were presented with two types of sound patterns in separate conditions while they were instructed to read a book of their own choice. In Scale condition, the standard sound pattern consisted of tones belonging to A major scale whereas the deviant pattern changed the mode of the pattern into A minor scale. In Compressed condition, the standard and deviant patterns consisted of tones with no musical relationship according to the Western tradition; that is, all intervals were compressed whole tone steps. The frequency change separating deviants from standards was of equal magnitude in the two conditions. The deviants elicited a statistically significant MMN in musicians and non-musicians in both Scale and Compressed conditions. The MMN amplitude was larger in Scale than in Compressed condition in both subject groups. This suggests that pitch discrimination is facilitated when tones are embedded in simple frequency ratios sequences (the ones used by Western musical tradition) rather than in complex frequency ratio ones, irrespective of the degree of musical training.

FNN6

NUMBER COMPARISON AND THE MENTAL NUMBER LINE - A FMRI-STUDY

K. Willmes[1], S. Weis[3], S. Kemeny[2], S. Pollrich[3], and S. Erberich[3]*

[1]Dept. of Neuropsychology, [2]Dept. of Neuroradiology, and [3]Interdisciplinary Center for Clinical Research, University Hospital RWTH Aachen, Germany

Dehaene and Cohen (1995) have proposed an anatomo-functional triple-code model of number processing and arithmetic, 'locating' a visual number form in inferior ventral occipito-temporal areas bilaterally, a verbal word form in left perisylvian areas and an analogue magnitude representation ('mental number line') in inferior parietal areas, bilaterally. Evidence for a quantitative number representation has been provided e.g. by RT measurements in simple number comparison experiments yielding a stable numerical distance effect, i.e. improved discrimination between two numbers with increasing numerical distance. In a PET study using a regions-of-interest approach, Dehaene et al. (1996) have only found weak (non-significant) corroboration for left and right inferior parietal activations during a mental number comparison of two one-digit numbers. In this fMRI study (1.5 T Gyroscan NT, Philips; T2* sensitive GRE sequence; 15 transverse 7-mm slices) on n=10 right-handed male subjects we studied cerebral acitivations in a number comparison task of individual visually presented one-digit arabic numbers resp. number words being compared mentally to the standard '5' without overt response in contrast to a low level control condition, in which a small circle was presented centrally, in a box-car type run comprising six periods of 45 s each: control - digits - words - control - words - digits. We also examined under which conditions the mental number line is activated even without having to perform a

'semantic' task on the numerals. Each of the following three tasks were contrasted with the above control condition: (1) passive viewing of pseudo-digits resp. pseudowords (2) passive viewing of digits resp. number words (3) mental decision about a 'surface property' of the digits (axial symmetry) resp. number words (grapheme monitoring of the letter /e/). Simple contrast comparisons provide evidence for the inferior parietal lobule (BA 40) to subserve a quantity number representation in the number comparison task both for arabic digits and to a lesser, yet significant degree for number words. In addition, a widespread network of areas is activated comprising visual processing in lateral occipital areas bilaterally (including activation of the visual number form representation in the posterior inferior temporal gyrus), and lexical and conceptual semantic processing in middle (and superior) temporal cortices. In addition, widespread (pre-)frontal areas, pre-SMA and anterior cingulate are activated as well. There is definitely no mental number line activation for passive viewing of pseudowords and number words.

Dehaene S, Cohen L (1995). *Mathematical Cognition* 1, 83; Dehaene S, Tzourio N, Frak V et al. (1996) *Neuropsychologia* 34, 1097.

FNN7

EFFECT OF ANTIPSYCHOTIC DUG SULPIRIDE ON THE EEG ACTIVITY AND PSYCHOPHYSIOLOGICAL MEASUREMENTS

V.N. Sinitsky[1], G.M. Gruzdev[1], I.V. Tetko[2,3], and A.E P. Villa[3]*

[1]Institute of Social and Forensic Psychiatry, Frunzestr., 103, 254080, Kyiv, Ukraine,, [2]Bogomoletz Institute of Physiology, Bogomoletz str. 4, 252024, Kyiv, Ukraine, and [3]Institut de Physiologie, Université de Lausanne, Rue du Bugnon 7, Lausanne, CH-1005, Switzerland

The effect of the antipsychotic drug Sulpiride, a selective dopamime D2-receptor antagonists was studied in 22 healthy women of 24-44 years old. EEG recordings in international 10/20 system were performed before and one hour after oral treatment with Sulpiride. In addition to the spectral power distributions and spatial mapping of the spectral density of EEG rhythms we analyzed inter- and intra-hemispheres relations of electrical activity by using coherence functions. We monitored the reaction time and accuracy of the responses by a battery of simple sensorimotor tasks, that included choice reactions and tapping tests, and cognitive tasks, that included short-term visual memory tasks and tests for logical thinking. The blood pressure and heart rate were also monitored. The distribution of the EEG frequency bands was significantly altered by Sulpiride administration. In particular, at the level of the central frontal areas we observed an increase of power density of alpha-waves and slow potentials (theta-1, theta-2 and delta). This effect was more prominent in the right hemisphere. At the level of occipital areas Sulpiride provoked, in some subjects, an inversion of the hemispheric dominant power of alpha-rhythm with splitting of its spectrum into several harmonics. Another major effect of Sulpiride was the disruption of inter-hemispheric coherence, when observed in control condition. The choice reaction time between two signals was increased by the drug, but insignificant muscle relaxation was observed. It also produced a moderate decrease of the blood pressure and heart rate. These results suggest that reduction

of motivation and volitional activity produced by Sulpiride form specific patterns of EEG activity. We raise the hypothesis that similar patterns as well as similar psychophysiological measurements can reveal impairment of the dopaminergic pathways at a pre-clinical stage.
Partially supported by a INTAS-OPEN 97-0173 grant.

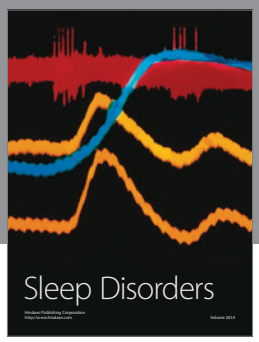
FNN8

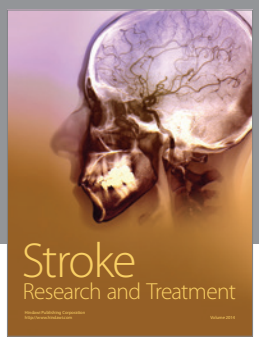
COGNITIVE LATERALIZATION: SEX DIFFERENCES IN EEG ASYMMETRY

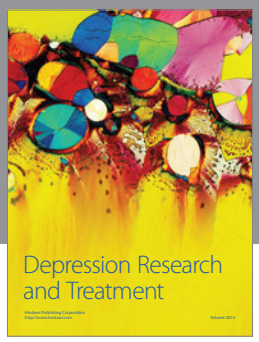
C. Persegani, P. Russo, E. Pettinelli, M. Torlini, M. Nicolini, C. Carucci, L.L. Papeschi, and M. Trimarchi*
Brain Health Centre, Centre of Clinical Neuropsychophysiological Research, Rome, Italy

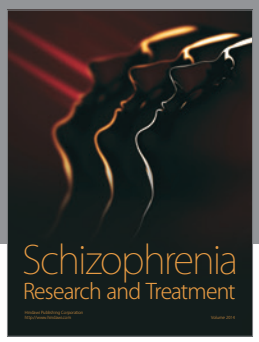
Several authors have suggested that individuals may differ in the extent to which they employ the processing abilities of one hemisphere rather than of the other hemisphere (1,4). This characteristic has been termed hemisphericity or hemisphere preference (HP) or, more in general, cognitive lateralization. The Preference Test (PT) is a paper-and-pencil test developed by Zenhausern (5) which intends to measure the HP. PT scores have already been correlated with frontal alpha power asymmetry derived from resting EEG performed on a younger female sample (2). PT scores have also been found to be linked to affective and neurotic symptoms. In a previous study, we have examined on a sample of 1,057 students, the sex differences in hemisphere preference by an Italian version of PT, providing some indications of a less pronounced lateralization of hemisphere-linked cognitive abilities in women (3). In the present study, we preliminarily evaluated if there were sex differences in alpha power asymmetry correlation with PT scores. For this purpose, we recorded the resting EEG and obtained PT score. Also a depression score by Zung Depression rating scale (Zung SDI) and anxiety score by State-Trait Anxiety Inventory (STAI) were measured. Our findings obtained on an adult sample replicate the results of previous observations, showing a correlation of PT scores with frontal, but not parietal, asymmetries in alpha power. However the correlation between PT scores and frontal asymmetry shows to be higher (>0.7) than in previous observations, without evidence of sex differences. In other words, subjects with a PT-defined left-hemisphere preference display relatively higher right- than left-hemisphere alpha power (i.e. a left-hemisphere activation) and vice versa. Although frontal asymmetries in resting EEG were related with individual differences in affective style, no significant differences emerged through the comparison of Zung SDI and STAI scores of subjects with left-HP respect to subjects with right-HP. In conclusion, this preliminary experimental observation supplies further evidence of connection between PT and frontal EEG asymmetries. Right-HP did not show to be associated with anxiety or depression increase respect to left-HP. Despite right-HP is frequently associated with anxious or depressive symptoms, our study does not support this observation.

(1) Hellige, J.B. (1990) *Ann. Rev. Psychol.*, 41:55; (2) Merckelbach *et al.*, (1997) *J. Clin.Psychol.*, 53:739; (3) Russo *et al.*, (1999) *Int. J. Neurosci.* (in press); (4) Trimarchi & Papeschi (1986) *Int. J. Psychophysiol.*, 4:263; (5) Zenhausern (1978) *Bull. Psychon. Soc.*, 12:381.









Hindawi
Submit your manuscripts at
http://www.hindawi.com