The abstracts are only available online, free of charge,
under www.karger.com/doi/10.1159/000095499

14th Biennial Congress of the International Pharmac-EEG Society (IPEG)

Awaji Island, Japan, September 7–10, 2006

Abstracts

Chairman
Toshihiko Kinoshita, Osaka

Contents

Session 1 Neurology	22
Session 2 IPEG Guidelines	25
Session 3 ERP Approach to Memory and Inhibitory Function	26
Session 4 Epilepsy	28
Session 5 Pharmac-EEG	30
Session 6 Neuro-Imaging in Psychiatry	32
Session 7 Past, Present and Future of Pharmac-EEG as a Biomarker	34
Session 8 Aroma	37

KARGER

Basel • Freiburg • Paris • London • New York •
Bangalore • Bangkok • Singapore • Tokyo • Sydney

Session 1: Neurology

S1-1

Memory Trace as Reflected by Mismatch Negativity

Hirooki Yabe

Department of Neuropsychiatry, Hirosaki University School of Medicine, Hirosaki, Japan

Pre-attentive change-detection system has been revealed in audition by studying the mismatch negativity (MMN) and its magnetic counterpart (MMNm). The main generator of MMN is located in the vicinity of the primary auditory cortex. MMN is elicited by the occasional change of repetitive sounds. The elicitation of MMN requires the sensory memory which keeps the information on various elements of repetitive sounds for detecting an incoming deviant sound. That is, MMN is generated by the comparison process between the deviated sound and the neural trace of the frequent sound stored in sensory memory. This 'memory trace' theory has been supported by a large amount of researches. Auditory sensory memory is strongly related to the brain mechanism termed the temporal window of integration (TWI) which integrates the closely presented sounds into single information units. Our previous studies have provided evidence for the presence of temporal integration system in sensory memory. MMN to omission in repetitive tones were elicited only with SOAs shorter than 160 ms. It suggested a temporal correspondence between the duration of the neural sound representations in sensory memory and the TWI of 160–170 ms. Sound trace might be represented as time-functional information or transient neural representation of the 160–170 ms auditory scene. We recently reported that the sensitivity for the deviation nonlinearly declines over time within the duration of sensory memory as reflected by TWI of 160–170 ms by showing that the MMNm peak amplitude was attenuated and MMNm peak latency was delayed for the later deviant omission of the stimulus. In the other study, more interestingly, the encoded (i.e., stored in the sensory memory) period from early to late omitted segment embedded in the sound of 170 ms in duration was shorter than the actual one. It suggested that time might be compressed in the neural representation of the auditory scene stored in sensory memory. Those studies demonstrated a temporal correspondence between the

short auditory sensory memory store, and the neural sound representations in sensory memory assumed to underlie the TWI. The study of sensory memory has many basic and clinical applications, because of its several advantages. It is important to make out how the sensory memory automatically forms auditory perceptual units along with the temporal integration function.

S1-2

Brain Imaging in Dementias

Ken Nagata, Tomoaki Kameda, Yosuke Nakamura, Takashi Yamazaki, Naoko Ogura, Taizen Nakase, Tetsuya Maeda, Yuichi Satoh, Mika Sato, Yasushi Kondoh, Kazuhiro Takahashi, Hirohiko Saito

Department of Neurology, Department of Radiology and Nuclear Medicine, Research Institute for Brain and Blood Vessels, Akita, Japan

In addition to the usefulness of structural brain imaging with x-ray CT and MRI, functional brain imaging such as single photon emission computerized tomography (SPECT) and positron emission tomography (PET) provides important physiological information in the diagnosis of dementias from the metabolic and/or hemodynamic point of view. Because of the depression in acetylcholine (ACh) neurotransmission in patients with Alzheimer's disease (AD), acetylcholinesterase (AChE) inhibitors are mainly used in the treatment of AD patients, and the efficacy of those AChE inhibitors is now being verified in those with vascular dementia (VaD) in clinical trials. The significance of the treatment with AChE inhibitors depends on the integrity of the ACh receptors in the dementias. For the imaging of the muscarinic ACh receptors (mAChR), we have developed a new ligand, ¹¹C-3-N-methyl-pierizil-benzilate (3-NMPB), for the positron emission tomographic (PET) imaging. In order to clarify the integrity of mAChR in VaD and AD, PET imaging with 3NMPB was performed in 8 patients with probable VaD based on NINDS-AIREN criteria and 13 patients with probable AD based on NINDS-ADRDA, and 10 age-matched normal volunteers served as normal control (NC). The mAChR binding was compared by the ratios compared with the cerebellum which were calculated from the regions of interest (ROI), and by three-dimensional statistic

analysis. Compared with the NC group, mAChR was not significantly reduced in any ROI in AD patients. In those with VaD due to cortical lesions, mAChR was reduced in the infarcted areas. On the other hand, mAChR was significantly reduced in the thalamus and anterior cingulate gyrus, but not in other cerebral cortices in patients with VaD due to subcortical lesions. Accordingly, it is suggested that mAChR is preserved in the cerebral cortices in patients with VaD due to subcortical lesions as well as in AD patients. The preservation of mAChR in mild to moderate AD patients as well as in subcortical VaD patients may endorse the efficacy of AChE inhibitors in the treatment of AS and VaD patients.

S1-3

Usefulness of ERPs for Evaluation of Dementia

H. Tachibana^a, M. Takeda^b, K. Kawabata^a, H. Nishimura^c

Departments of ^aGeneral Internal Medicine, ^bNeurology, Hyogo College of Medicine, ^cDepartment of Neurology, Nishinomiya Kyoritsu Noshinkeigeka Hospital, Nishinomiya, Japan

Background/Objectives: Long-latency event-related potentials (ERPs), which index the nature and timing of a cognitive response to a stimulus, are one approach to assessing cognitive function. In particular, the P300 component is considered to be an electrophysiological parameter of certain cognitive process. In this study, we investigated the possible usefulness of ERPs for evaluation of patients with cognitive impairment or dementia. **Methods:** (1) Auditory ERPs were recorded in an oddball paradigm using auditory stimulation in patients with Binswanger's disease and Alzheimer's disease (AD). (2) ERPs were recorded during the performance of visual discrimination tasks using three kinds of stimuli in patients with Parkinson's disease (PD), AD and multiple lacunar infarcts (MCI). Each component of P300 response to infrequent non-target stimuli and P300 response to infrequent target stimuli was defined as P3a or P3b. (3) To analyze chronometrically the possible cognitive slowing in PD, visual ERPs and reaction times (RTs) were measured during the performance of semantic discrimination tasks. The components of the N1, P2, NA, N2 and P3 and simple and GO/NOGO RTs were observed. **Results:** (1) Both groups with dementia showed significant prolongation of N200 and P300 latencies compared with normal controls. (2) In patients with PD with dementia, no significant prolongation was found in the P3a latency although most of PD patients showed prolongation of P3b latency. On the other hand, patients with AD showed significant prolongation of both the P3a and P3b latencies compared to the normal controls. The P3a latency in patients with MCI was significantly longer than that of the normal controls, while no significant differences could be found in P3b latency between MCI patients and normal subjects. A significant correlation was found between P3a latency and frontal cortical blood flow. (3) The N2 and P3 latencies and GO/NOGO RT in patients with PD were significantly longer than those in the controls, although there were no differences in N1, P2 and NA latencies or simple RT between the patients and normal controls. **Conclusion:** The P3 response could be helpful in the

evaluation of patients with dementia, although other components should be investigated to clarify more detailed analysis of information processing. The ERP study may be useful in the differentiation of the dementia etiologies which have different electrophysiological features that may be related to their underlying pathologic mechanisms.

S1-4

ERP Latencies, Amplitudes and Loreta Sources in Vascular and Degenerative Dementia before and after Nicergoline Therapy

P. Anderer, B. Saletu, H.V. Semlitsch, G.M. Saletu-Zyhlarz

Department of Psychiatry, Medical University of Vienna, Vienna, Austria

Background/Objectives: Clinical and Q-EEG methods revealed nicergoline (NIC) to be significantly superior to placebo (P) in improving psychopathology and vigilance in dementia. For evaluation of cognition, middle latency and late components of event-related potentials (ERPs), reflecting perceptual and cognitive information processing, were utilized. **Materials and Methods:** In 112 patients with mild to moderate dementia (aged 60–91 years; 56 senile dementia of the Alzheimer type (SDAT), 56 multi-infarct dementia (MID)), ERPs were recorded before and after 8-week treatment with 2 × 30 mg NIC or P. **Results:** As compared with healthy controls (n = 18), both SDAT and MID patients showed delayed pretreatment target ERP latencies and increased standard ERP amplitudes. Low-resolution brain electromagnetic tomography (LORETA) revealed that demented patients allocated sources for the attentional orientation system at earlier stages (structural differences) and showed increased source strength for perceptual (auditory) and cognitive (event-encoding) processes (energetic differences). Correlation analysis between measures of 'cognitive dysfunction' (SCAG-1) and LORETA sources showed this compensatory reallocation of resources only in mild dementia. NIC shortened P300 latency (improvement of stimulus evaluation time) and induced – compared with P – changes opposite to the differences observed in LORETA ERP source strength between untreated demented patients and normal controls. **Conclusion:** Mildly demented patients use additional neuronal resources to compensate for losses attributable to the disease. NIC tends to normalize the deviant brain function in MID and SDAT patients (key-lock principle in the diagnosis and treatment of mental disorders), which leads to clinical improvement (CGI, SCAG and MMS scores).

S1-5

Effects of Donepezil Hydrochloride on P300 and Cerebral Blood Flows in Alzheimer's Disease

Minoru Oishi

Department of Neurology, Nihon University Nerima
Hikarigaoka Hospital, Tokyo, Japan

Background/Objectives: In Alzheimer's disease, the P300 latency has been reported to be prolonged and cerebral blood flows have been reported to be decreased. On the other hand, donepezil hydrochloride has been used to treat Alzheimer's disease. Although donepezil hydrochloride does not stop the progression of Alzheimer's disease in the long run, it may improve the symptoms of Alzheimer's disease for a few months. Therefore, the P300 latency and cerebral blood flows were measured before and eight weeks after the start of donepezil hydrochloride therapy. **Materials and Methods:** Twelve patients with Alzheimer's disease were investigated after getting the informed consent. The mean age of the patients was 64 years. All the patients were investigated with voxel-based specific regional analysis system for Alzheimer's disease (VSRAD) and meta-iodobenzylguanidine (MIBG) cardiac scintigraphy. The P300 latency was measured according to the guideline of the Japanese Society of Clinical Neurophysiology. Cerebral blood flows were measured with single photon emission computed tomography (SPECT). **Results:** The P300 latency after the start of donepezil hydrochloride therapy was significantly shorter than that before the start of donepezil hydrochloride therapy. The temporal cortex blood flow and parietal cortex blood flow were significantly increased after the start of donepezil hydrochloride therapy in comparison with those before the start of donepezil hydrochloride therapy. **Conclusion:** Donepezil hydrochloride may shorten the P300 latency and increase cerebral blood flows in Alzheimer's disease.

S1-6

Visual Evoked Potentials in Creutzfeldt-Jakob Disease

Shigeru Koyano, Hiroyuki Toda, Yoshiyuki Kuroiwa

Department of Neurology, Yokohama City University School of Medicine, Yokohama, Japan

Background/Objectives: Neuropathological studies show frequent and extensive effects on the visual system in Creutzfeldt-Jakob disease (CJD), but deterioration of vision is not reported by all patients. The Heidenhain variant is a subtype of CJD where visual symptoms are leading. We examined the function of the visual system by means of visual evoked potentials (VEP) in combination with symptoms and MRI in Heidenhain variant of CJD. **Materials and Methods:** Bionocular VEP responses to flash stimulation (250 lux) at a rate of 1 Hz were recorded. The three patients (2 women and 1 man) with a mean age of 70 years (range 62–80 years) were given a diagnosis of sporadic 'probable CJD' on the basis of standard criteria (WHO Consultation, 1998). All disease courses were from 3 to 6 months after first symptoms occurred, progressive stages. **Results:** *Symptoms and MRI:* None of the patients had fam-

ily history for CJD, history of traveling or organ transplantation history. During the course of the disease visual symptoms, vertigo haze, pseudopsia appeared in 2 of 3 patients. Cerebral spinal fluid (CSF) examination revealed the presence of 14-3-3 protein and high concentrations of NSE in all patients. DNA analysis performed to detect the presence of PrP gene mutation were negative. The degree of brain atrophy in three patients was various by MRI, and the showing atrophy of occipital lobe by diffusion weighted image was only one. Repeated EEGs showed generalized, diffuse slowing and occasionally periodic synchronous sharp waves (PSD) in all patients. *VEP:* All patients had normal wave form and pathological VEP with a delayed P100 component or large amplitudes (10–80 μ V), 'giant VEPs' with a laterality by bilateral irritation. The patients with visual impairment and those without were not different concerning VEP findings. **Conclusion:** 'Giant VEP' showed to relate to brain atrophy than clinical symptoms and MRI findings. We suggest that it may reflect the cerebrocortical excitability and extrapyramidal effect. A laterality of amplitudes by bilateral irritation may reflect a lesion of a retina and optic nerve. These results point to an early effect on the visual system in CJD, irrespective of clinical visual deficits.

S1-7

Neurophysiological Approach to Visual Hallucinations in Dementia with Lewy Bodies and Parkinson's Disease with Dementia

Akira Kurita

Department of Neurology, Jikei University School of Medicine, Tokyo, Japan

Background/Objectives: Visual hallucinations (VHs) are common in dementia with Lewy bodies (DLB) and Parkinson's disease (PD) with dementia (PDD), while auditory ones are relatively rare in these neurodegenerative disorders. Recent epidemiological studies have shown an association between visual impairments and VHs in PD patients, and neuropsychological studies have revealed visuoperceptual impairments in hallucinatory patients with DLB and PDD. Radionuclear studies have demonstrated decreased blood flow in the posterior lobe in these disorders. Based on these findings together, it is possible to speculate that visual functions including primary ones and information processing are specifically impaired in DLB and PDD, contributing, in part, to the pathophysiology of VHs. To clarify the association between visual information processing functions and VHs, we compared DLB, PDD and Alzheimer's disease (AD) patients with visual event-related potentials. Also, recent neurophysiological investigations regarding the VHs and visual functions in DLB and PD/PDD were reviewed. **Materials and Methods:** In our study, we compared visual P3 event-related potential (VP3) latencies among patients with PDD with (PDD-H: 11) and without VHs (PDD-N: 6), DLB (24) and AD (21), and healthy volunteers (C: 20), with consideration of auditory P3 (AP3) latencies. The mean ages and MMS scores of the 4 patient groups were comparable. To elicit VP3s and AP3s, a visual paradigm with human faces and a conventional auditory odd-ball paradigm were used, respectively. In the review, we investigated neurophysiological

studies on the association between VHs and visual functions in DLB and PDD published over the past 10 years. **Results:** In our study, all of the 4 patient groups had significantly longer VP3 and AP3 latencies than the C group. The mean VP3 latencies in the PDD-H and DLB groups, but not in the PDD-N group, were significantly longer than that in the AD group, while the mean AP3 latencies in those 4 patient groups were comparable. The review of the literature revealed that there were only 2 studies neurophysiologically investigating the association between VHs and visual functions in DLB or PD patients. In one study, the mean P100 latency of visual evoked potentials (VEPs) was significantly longer in the PD patients with VHs than that in the patients without VHs. In the other study, abnormal vision and abnormal visual P3 latencies did not correlate with the incidence of VHs in PD patients during the 8-year follow-up period. **Conclusions:** Our findings and the result of the study with VEPs together suggest that both primary visual functions and visual information processing are impaired in hallucinatory patients with DLB and PDD. Our findings also suggest that disproportion between visual and auditory cognitive functions is characteristic of PDD-H and DLB. VHs might be associated in part with predominating visual cognitive impairments in PDD-H and DLB patients.

S1-8

Antiparkinsonian Drugs' Effects on Frontal Lobe Function

Mikio Osawa

Department of Neurology, Tokyo Women's Medical University, Tokyo, Japan

Antiparkinsonian drugs, especially levodopa and dopamine receptor agonists, affect not only motor symptoms but also mood disorders. Their responsible lesions are thought to be in the mesocortical/mesolimbic dopaminergic system, especially the frontal lobe. These regions are also thought to be the generator sources of event-related potentials (ERPs) evoked by nogo stimuli, i.e. nogo N2 and nogo P3. In PD patients, even at an early stage without dementia, the self-rating depression scale showed significantly higher scores than in normal controls; apathy scores exhibited a tendency to be higher; and the fatigue scale showed significantly higher scores. These scores were significantly correlated with each other. The nogo N2 amplitude correlated significantly with apathy and fatigue scores but not with SDS scores. In early PD patients without any sign of dementia at the early stage, levodopa improved the symbol digit modalities test significantly, suggesting that levodopa may influence attention and/or speed of information processing. Pramipexole significantly improved SDS, fatigue and apathy scores as well as motor symptoms, especially SDS and fatigue scores, suggesting that it influences function of the frontal lobe. Dysfunction of the frontal lobe can be recognized and improved with antiparkinsonian drugs in PD patients even at an early stage without any sign of dementia.

Session 2: IPEG Guidelines

S2-1

Guideline for Pharmac-Sleep Studies in Man

P. Anderer^a, B. Kemp^b

^aDepartment of Psychiatry, Medical University of Vienna, Vienna, Austria; ^bSleep Center, Westeinde Hospital, Den Haag, The Netherlands

Background/Objectives: This guideline, developed by an expert group whose members are P. Anderer (Vienna, Austria), B. Kemp (Den Haag, The Netherlands), M.J. Barbanj (Barcelona, Spain), H. Danker-Hopfe (Berlin, Germany), P. Drinkenburg (Beerse, Belgium), M. Jobert (Berlin, Germany), T. Kinoshita (Osaka, Japan), T. Penzel (Berlin, Germany), G. Ruigt (Oss, The Netherlands), B. Saletu (Vienna, Austria), L. Staner (Rouffach, France), T. Roth (Detroit, Mich., USA), H. Yamadera (Tama Nagayama, Japan) and G. Zammit (New York, N.Y., USA), is a supplement to the previous IPEG guidelines 'Guidelines for Pharmac-EEG Studies in Man' (1982), 'Recommendations for Standardization of Data Acquisition and Signal Analysis' (1987), 'Recommendations for EEG and Evoked Potential Mapping' (1990), 'Registration and Computer-Supported Evaluation of Pharmac-EEG Data' (1995) and 'IPEG Guideline on Statistical Design and Analysis for Pharmacodynamic Trials' (1999). The present guideline is intended to provide support for the design and analysis of pharmac-sleep studies in man with respect to selection of subjects and patients, environmental and situational factors, data acquisition, data format as well as macro- and micro-structural sleep analysis including standard sleep scoring according to Rechtschaffen and Kales. Moreover, the guideline covers continuous sleep analysis based on FFT analysis, analysis of physiological components of sleep by means of sleep-dependent neuronal feedback loops and continuous probabilistic models of the sleep process, analysis of additional biosignals, actigraphic analysis and reporting of data. According to the goal of this guideline, it contains comments and recommendations specifically designed for pharmac-sleep studies.

S2-2

Guideline for the Use of qEEG Results

R. Luthringer^a, W. Drinkenburg^b, P. Boeijinga^a, L. Prichep^c, L. Soufflet^a

^aFORENAP Pharma, Rouffach, France; ^bDepartment of Psychology, University of Nijmegen, The Netherlands;

^cBrain Research Laboratories, Department of Psychiatry, New York University School of Medicine, New York, N.Y., USA

With the rapid advance of quantitative EEG techniques in the past two decades, the International Pharmac-EEG group (IPEG) has found necessary to publish guidelines on data acquisition, signal analysis and statistical methodology. Compliance with

these previous recommendations should help to a better homogenisation of methodological aspects between research teams and thus more relevant comparisons between results from different laboratories. As was already explained in the previous guidelines issued by IPEG, different ways to analyse the data (i.e. scalp vs. source localisation information, linear vs. non-linear approaches, ...) are nowadays available. The aim of the present guideline is to provide an expert view on how to interpret the different types of qEEG data generated during pharmacological trials at either the preclinical (i.e. animals), clinical pharmacology (i.e. mostly healthy subjects) or neuropsychiatric (i.e. neurological or psychiatric patients) stages.

Session 3: ERP Approach to Memory and Inhibitory Function

S3-1

Domain-Specific Organization of Auditory Working Memory

C. Alain

Rotman Research Institute, Baycrest Centre for Geriatric Care and Department of Psychology, University of Toronto, Toronto, Canada

Background/Objectives: Evidence from animal studies suggests that identification and localization of auditory objects, like visual objects, are sorted into specialized ventral ('what') and dorsal ('where') processing streams, respectively. Although this model has received considerable support from neuroimaging studies in humans, the functional role of these pathways in general and the dorsal pathway in particular remain controversial. The sensory-motor account posits that the dorsal brain regions (e.g., inferior parietal lobule, IPL) indexes sensory-motor integration required during 'where' responding. An alternative account suggests that the IPL plays an important role in monitoring sound location. The present set of ERP and fMRI experiments aimed to characterize the functional role of the 'where' system in auditory working memory. **Materials and Methods:** Participants were presented with environmental sounds chosen randomly from three possible semantic categories (e.g., man-made, animal, music) and three possible locations (e.g., left, center, right). They performed an n-back task in which they pressed a button when the same location (where task) or the same semantic category was repeated. **Results:** The analysis of fMRI data revealed greater activity in the right IPL during the location task than in the category task while taking into account activity related to target processing, suggesting that the IPL play an important role in monitoring and updating sound location in memory. Both location and identity targets generated enhanced signal in the postcentral gyrus, prefrontal cortex and parietal cortex. The analysis of ERP data revealed location-specific activity at about 250 ms following sound onset, which was slightly lateralized over the right hemisphere. **Conclu-**

sion: Together, these findings provide strong support for domain-specificity of auditory working memory. In addition, our results favor a working model that, although specialized for processing 'what' and 'where' information separately, utilizes a common network during participants' responses.

S3-2

The Development of Memory Trace as Reflected by the MMN

Takashi Matuoka, Hirooki Yabe, Ren Asai, Etsuko Hara, Sunao Kaneko

Department of Neuropsychiatry, Hirosaki University School of Medicine, Hirosaki, Japan

The mismatch negativity (MMN), an event-related potential (ERP) component, is elicited when an auditory deviant stimulus interrupts a regular sequence of standard stimuli, even in the absence of attention. Näätänen proposed the memory trace hypothesis that MMN reflect a neuronal mismatch process between deviant (infrequent) auditory input and the sensory memory trace representation of the standard (frequent) stimulus. Although many previous studies have investigated MMN to reveal sensory memory mechanism, the development of memory representation still remains unclear. We studied how the development of memory trace affect the response of the MMN. We carried out two experiments. In these experiments, the way to the formation of the standard stimulus representation varied in each condition. One experimental design is that the number of the standard stimuli was different for each condition. This design enabled the investigation of the sensory memory without the effect of the preceding train (i.e., the influence of long-term memory). When the number of standard stimuli was 1, 3, 5 or 7, we measured the frontal and the temporal MMN components, respectively. Furthermore, we used whole-head 204-channel magnetoencephalography (MEG) to record the brain's magnetic fields elicited by the deviant stimuli that occurred as the 4th, 6th and 8th stimulus after the initial standard stimulus. The result is that the amplitude of the frontal MMN and temporal MMN was significantly enlarged when the number of the standard stimuli preceding the deviant stimuli was increased. Moreover, the latencies of both MMN components were significantly shortened. Another experimental design is that the change of deviant-stimulus probability (5, 20, 40% 45, 47 and 50%) was different for each condition. Furthermore, we explored the topographical aspect of MMNm (magnetic counterpart of MMN) by using MEG. We found not only the significantly enhanced amplitude of frontal MMN but also the significantly shortened latency for both MMN components when the probability of standard stimuli was increased. Furthermore, we found the significantly enhanced amplitude of temporal MMNm component when the probability of standard stimuli was increased. However, the effect on the temporal MMN was smaller than the frontal one.

S3-3

Functional Characterization of Mismatch Negativity to a Visual Stimulus

T. Maekawa, S. Tobimatsu

Department of Clinical Neurophysiology Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Objective: To record visual mismatch negativity (V-MMN) to a windmill pattern that fulfills similar criteria as that of auditory MMN (A-MMN). **Methods:** Twelve normal adults were instructed to listen to a story and to also pay attention to a visual target. Windmill patterns consisting of a standard, a deviant, and a target stimulus whose ratios were 8:1:1 were presented randomly. The difference in the three stimuli was the number of vanes. To ensure endogeneity, the standard and deviant stimuli were alternated. To vary the difference between the frequent (standard) and infrequent (deviant) stimuli, the deviants were changed by modulating the number of vanes. To examine the effect of physical features of the target stimulus on changes in detection, two target conditions were used. To elucidate the presence of sensory memory, additional experiments were performed. Train bursts that consisted of one deviant and eight standard stimuli were presented repeatedly, changing either inter-trains interval or changing the sequence. The deviant-related component (DRC) was obtained by subtracting the event-related potentials (ERPs) to the deviant stimulus from that to the standard stimulus. **Results:** Seven subjects completed all phases of the experiment. Behavioral performances indicated that the subjects' attention was directed to the auditory context and identification of the target stimulus. The DRC appeared 150–300 ms after the stimulus onset and consisted of an early (DRN1) and a late (DRN2) component. The magnitude of deviancy from the standard stimulus significantly influenced the latency of DRN2 but not its magnitude, while a change of the target stimulus affected the latencies of both DRN1 and DRN2. **Conclusions:** Our DRCs satisfied the criteria of A-MMN. In contrast to A-MMN, only the latency of the DRC is associated with visual sensory discrimination and attentional reorienting.

S3-4

Investigation of Somato-Motor Inhibitory Processing in Humans Using Go/No-Go Paradigm

H. Nakata, R. Kakigi

National Institute for Physiological Sciences, Okazaki, Japan

Background: The go/nogo task is a useful paradigm for recording event-related potentials (ERPs) to investigate the neural mechanisms of response inhibition. In nogo trials, a negative deflection at around 140–300 ms (N2), which has been called the 'nogo potential', is elicited at the frontocentral electrodes, compared with ERPs recorded in go trials. In the present study, we investigated the generators for nogo potentials by recording ERPs and magnetoencephalography (MEG) simultaneously during somatosensory Go/No-go tasks. **Materials and Methods:** Eight nor-

mal right-handed subjects participated in this study. The subjects performed a warning stimulus (S1) – imperative stimulus (S2) paradigm with Go/No-go tasks. S1 was an auditory pure tone. For the S2, we stimulated the second or fifth digit of the left hand with ring electrodes. The recordings were conducted in three conditions. Condition 1 was the resting control. In condition 2, the go stimulus was delivered to the second digit of the left hand, and the nogo stimulus to the fifth digit of the left hand. The subjects had to respond to it by pushing a button with their right thumb as quickly as possible only after the presentation of a go stimulus. In condition 3, the go and nogo stimuli were reversed in the left hand. EEGs were recorded at Fz, Cz, Pz, C3, C4, F3 and F4. MEG signals were recorded with a helmet-shaped 306-channel detector array (Vectorview; ELEKTA Neuromag Oy, Helsinki, Finland). The signals were recorded with a bandpass of 0.1–100 Hz and digitized at 900 Hz. **Results:** ERP data revealed that the amplitude of nogo-N140 component, which peaked at about 155 ms from frontocentral electrodes, was significantly more negative than that of go-N140. MEG data revealed that a long-latency response peaking at approximately 170 ms, termed nogo-M170 and corresponding to nogo-N140, recorded in only nogo trials. The equivalent current dipole (ECD) of nogo-M170 was estimated to lie around the posterior part of the inferior frontal sulci in the prefrontal cortex. These results revealed that both nogo-N140 and nogo-M170 evoked by somatosensory Go/No-go tasks were related to the neural activity generated from the prefrontal cortex. **Conclusion:** Our findings combining MEG and ERPs clarified the spatial and temporal processing related to somato-motor inhibition caused in the posterior part of the inferior frontal sulci in the prefrontal cortex in humans.

S3-5

Neural Correlates for Memory of Novel Events in Human

H. Bokura, S. Yamaguchi

Department of Neurology, Shimane University, Faculty of Medicine, Izumo, Japan

Objective: Differences in Novelty event-related potentials (ERPs) for incidental and intentional memory retrieval were studied. **Methods:** We recorded ERPs in eleven healthy volunteers using a high density 128-sensor net. Subjects performed a novelty oddball task, in which triangles were presented on a computer screen (standard stimuli), leaned triangles were for target stimuli, and novelty pictures were randomly inserted for novelty stimuli. Session 1, subjects were not indicated to memorize novelty pictures (incidental retrieval). Session 2, subjects were indicated to memorize novelty pictures intentionally (intentional retrieval). After each session, pictures (half of them were repeated) were represented at random. Subjects were requested to judge whether it was presented before or not. We analyzed the differences of Novelty Negativity component between remembered pictures or not. **Results:** The mean correct rate for remembering pictures for incidental and intentional retrieval was 64 and 78%, respectively. There were no differences in latency or amplitude regarding Novelty Negativity (mean latency was 260 m/sec) between successful and unsuccessful

incidental encoding. On the contrary, as for intentional encoding the Negativity for remembered pictures were significantly longer latency and larger amplitude than those for not remembered. These effects were maximal at the frontal lobe. **Conclusions:** The results suggest that the frontal N2 component is involved in intentional encoding of novel events but not in incidental encoding.

S3-6

Memory Function Evaluated by ERP Old/New Effects during a Recognition Memory Paradigm

H. Tachibana^a, Y. Kida^b, M. Takeda^b, K. Kawabata^a

^aDepartment of General Internal Medicine, ^bDepartment of Neurology, Hyogo College of Medicine, Nishinomiya, Japan

Background/Objectives: Many studies have used event-related potential (ERPs) to investigate the cognitive processes involved in direct and indirect memory tests. In both kinds of tests, the most consistent findings is that ERPs evoked by the first presentation of a stimulus (i.e., new stimulus) are relatively less positive than those elicited by the second presentation of the same item (i.e., repeated stimulus). This modulation is termed as 'ERP repetition effect' or 'ERP old/new effect'. In the present study, we investigated electrophysiological correlates related to the recognition of repeated unfamiliar faces during a recognition memory task. **Materials and Methods:** Twenty young healthy adults (mean age 24.5 years), 15 elderly healthy adults (mean age 65.0 years) and 15 patients with Parkinson's disease (PD) (mean age 63.4 years) participated in this study. To elicit ERPs, unfamiliar faces were repeated immediately after initial presentation (at lag 0), after one intervening face (lag 1) or at lag 3. Subjects were requested to push a button with the right thumb upon first presentation of a face and with the left thumb upon repeated presentation. **Results:** Compared to the young healthy adults, the accuracy of old/new responses for the first presentation of unfamiliar faces was decreased in elderly healthy adults and decreased even more in patients with PD, while no significant differences were seen for repeated faces between patients with PD and elderly healthy group. Compared to the young healthy group, the elderly healthy group had prolonged reaction times (RTs) for both the first and repeated faces. However, there was no significant difference in RTs for new and repeated faces between the elderly healthy group and patients with PD. Both the control groups and patients with PD showed a significant RT priming effect at the lag 0 repetition, which in all groups, RTs in the lag 3 repetition were delayed relative compared to new faces. ERP amplitude between 300 and 500 ms after the stimulus in both healthy subjects showed a positive shift for lag 0 at all sites and for lag 1 and lag 3 repetitions at the Fz site, while effects in the PD group were not noted in any site, even for the lag 0 repetition. ERP waveforms for the first presentation of faces in PD patients showed a significant positive shift compared to healthy groups. **Conclusion:** These data suggest that recognition memory for unfamiliar faces was impaired in advancing age and impaired even more in patients with PD. In addition, recognition memory deficits in PD may result, at least partly from the impairment of context integration process.

Session 4: Epilepsy

S4-1

QEEG Source Localization of Epileptiform Foci

L.S. Prichep^{a, b}, K. Alper^{a, c}

^aBrain Research Laboratories, Department of Psychiatry, NYU School of Medicine, New York, N.Y., ^bNathan S. Kline Institute for Psychiatric Research, Orangeburg, N.Y.,

^cComprehensive Epilepsy Center, NYU School of Medicine, New York, N.Y., USA

Scalp recorded ictal and interictal EEG have contributed little to the localization of epileptogenic foci in patients with partial epilepsy. While neuroimaging techniques such as MRI, SPECT, and PET can be used to localize structural or metabolic dysfunction, they do not correlate well with neurophysiological dysfunction. Intracranial EEG recordings are therefore often required to identify epileptogenic regions. Non-invasive quantitative techniques that facilitate localization of such dysfunctional areas of the cortex would have significant clinical utility. In this study, source localization of the scalp recorded EEG was used to identify epileptiform foci in interictal EEGs. Results were compared with localization from invasive intracranial EEG recordings. **Patients and Methods:** Six adult patients (3M, 3F) who had undergone invasive intracranial EEG monitoring at the *New York University Comprehensive Epilepsy Center* were selected for study. The mean age of the study group was 32.7 years (age range 23–44 years). Patients with both unilateral and bilateral seizure onsets were included, but those with previous invasive procedures were excluded. Two minutes of artifact-free eyes closed resting EEG were selected for analysis, from 19 lead recordings referenced to linked ears. Using norms for narrow band spectral power, Z transformed spectra were computed. The maxima of the Z-spectra in the slow wave range was selected as the frequency of the main source. Both Variable Resolution Electromagnetic Tomography (VARETA) and Low Resolution Electromagnetic Tomography (LORETA) were used to identify sources from the scalp recorded EEG, blinded to the findings from invasive methods. In addition, results were compared with MRI findings, visual inspection and QEEG. **Results:** The source images in the delta-theta frequency range correctly identified epileptogenic regions in all of the 6 patients studied, using either VARETA or LORETA methods. In comparison, visual inspection of the EEG correctly localized the hemisphere of dysfunction in 5 patients, but only localized epileptic dysfunction to a specific region in 1 patient. Similarly, QEEG Z-images lateralized the focus in 2 patients, while localization to a specific region was possible in only 1. MRI found localized lesions in only 2 patients, correctly localizing the hemisphere, but not the specific region. **Conclusions:** The agreement between source localization of the scalp recorded EEG with intracranial EEG is encouraging, and points the way to future studies in larger populations of patients. The apparent localizing accuracy of VARETA and LORETA applied to non-epileptiform background activity may be especially suited for non-lesion epileptic patients whose scalp EEG's show a paucity or absence of epilepti-

form abnormalities and non-localizing ictal patterns. This method, used in conjunction with EEG recordings routinely acquired in the course of clinical evaluations, represents a non-invasive technique for localizing information which may be an important adjunct to the conventional methods currently in use.

S4-2

Topographic Movie of Ictal High-Frequency Oscillations on the Brain Surface Using Subdural EEG in Neocortical Epilepsy

Tomoyuki Akiyama

Department of Child Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Objectives: Multiple-Band Frequency Analysis (MBFA) has higher temporal and frequency resolutions than conventional power spectral analyses. To study rapid dynamic changes of high-frequency oscillations (HFOs) in neocortical epileptic seizures, we integrated MBFA into brain-surface topographic mapping. **Materials and Methods:** We studied two patients with intractable neocortical epilepsy by subdural EEG (SDEEG) at a 1 kHz sampling rate at the Hospital for Sick Children, Toronto. For each electrode in SDEEG, we conducted an MBFA for the EEG sections at seizure onset with 1 Hz and 10 ms resolutions, identified the prominent frequency range of HFOs, and averaged HFO powers in that range. We made color topographic maps of the averaged HFO powers and superimposed them on the brain-surface digital photographs. We converted consecutive topographic maps (10 ms each) to movie files. Case 1: a 17-year-old girl with focal sensory-motor seizures in the right hand with secondary generalization. Case 2: a 14-year-old boy with asymmetric epileptic spasms in clusters. **Results:** In Case 1, during focal seizures the topographic movie revealed that high-power HFOs (60–120 Hz) initially emerged at the superior portion of the left precentral gyrus, then shifted to the left postcentral gyrus, and subsequently reverberated between both regions and also the posterior portion of the left postcentral gyrus. In Case 2, during each spasm the movie demonstrated that high-power HFOs (80–120 Hz) initially emerged at the left superior frontal gyrus and subsequently spread over the left inferior frontal and middle temporal gyri. **Conclusion:** The brain-surface topographic movies of HFOs disclosed that multiple cortices cooperated to generate seizures in multiple and complex ways in the neocortical epilepsy.

S4-3

Epileptic Focus Detection Using Multi-Channel Intracranial Electrodes and 3-D MRI

Madoka Yamazaki

Department of Life Sciences and Bio-informatics, Tokyo Medical and Dental University, Tokyo, Japan

Objective: Intracranial digital electrocorticography (ECoG) monitoring with multi-channel electrodes is frequently used to delineate the epileptogenic zone in patients with neocortical epilepsy. I evaluated the clinical value of computerized voltage topographic mapping of ictal spikes superimposed over photographed grids and 3-D MRI and will demonstrate this analysis of ictal ECoG with a simultaneously recorded video. **Methods:** We applied computerized topographic analysis of ictal spikes using subdural and 3d-mri images to define epileptic zone to two patients with intractable frontal lobe epilepsy and one patient with intractable lesional parietal lobe epilepsy (case 1). The spike voltage topographic maps (vt map) were created on an electrode template of the cortical surface grids and 3d-mri using a review program (insight) and an analysis program (prism; persyst, az). In case 3, we also analyzed the ictal spikes by the continuous wavelet method. **Results:** In case 1, the ictal discharge was localized to one electrode just above the tumor. In cases 2 and 3, the ictal discharges appeared simultaneously on many channels. The vt map revealed the extent of ictal discharges, which enabled us to recognize the zone of the ictal onset and the time course of the discharge propagation. In case 3, the vt map represented a broadly distributed epileptogenic zone, and the continuous wavelet analysis made the ictal onset zone to localize clearly. **Conclusion:** This method showed the ictal onset zone and its time course by the amplitude distribution of the ictal spike on the individual brain-surface images. The anatomical information of location, distribution and propagation of ictal spike discharges can provide the resection area of the epileptogenic zone in epilepsy surgery.

S4-4

SAM(G2) Analysis: A New Approach for MEG Source Localization of Epilepsy

R. Ishii^a, S.E. Robinson^b, M. Iwase^a, L. Canuet^a, R. Kurimoto^a, K. Ikezawa^a, M. Azechi^a, S. Ukai^d, T. Yoshimine^c, K. Shinosaki^d, M. Takeda^a

^aDepartment of Psychiatry, Osaka University Graduate School of Medicine, Japan; ^bVSM MedTech Ltd., CTF Systems, Coquitlam, Canada; ^cDepartment of Neurosurgery, Osaka University Graduate School of Medicine, ^dDepartment of Neuropsychiatry, Wakayama Medical University, Japan

Objectives: SAM(g2) analysis, a combination of Magnetoencephalography (MEG), Synthetic Aperture Magnetometry (SAM) and excess kurtosis (g2) method, is a novel epilepsy analysis procedure based on a spatial filtering technique. The aim of this study is to examine SAM(g2) analysis using MEG signals of the epilep-

tic patients. **Case:** A 35 years-old-male. At the age of 25, he had suddenly suffered from colored elementary visual seizure lasting several seconds, which were followed by generalized tonic clonic seizures (GTCS). He described many unformed sparkling blobs with various colors moving in the bilateral visual fields during the visual seizures. Although he is taking the anti-epileptic drugs, he still has these seizures several times a year. The patient provided written informed consent for the experimental procedures. **Methods:** The MEG signals were recorded five times in these eight years, and were analyzed using ECD analyses. SAM(g2) analysis also produced a three-dimensional image of the g2 values and automatically estimated spike localization from raw MEG epilepsy signals including spikes. **Results:** For the MEG signals at the first measurement, ECD analysis estimated most of the interictal spikes in the right fusiform and inferior temporal gyri, which subserve human color processing. SAM(g2) analysis also estimated the localization of interictal spikes activities in the same areas. From second to fifth measurements, both ECD and SAM(g2) analyses estimated them in the right transverse gyrus of Heschl. His clinical symptoms of colored elementary visual seizure ceased in accordance with the changes of the estimated localizations of the equivalent current dipoles (ECDs) of the interictal spikes in eight years observation with effective medication. **Conclusion:** As well as ECD analysis, SAM(g2) analysis successfully estimated the changes of the localizations of the interictal spikes in accordance with the changes of the patient's clinical symptoms, indicating that SAM(g2) analysis is useful for detection of interictal spike localization in epileptic patients.

Session 5: Phamaco-EEG

S5-1

Ethanol Effects on the Spatial Configuration of Brain Electric Activity

T. Isotani^{a,b}, D. Lehmann^c, R.D. Pascual-Marqui^c, L.R.R. Gianotti^c, P.L. Faber^c, J. Wackermann^d, A. Saito^{b,e}, T. Kinoshita^b

^aDepartment of Psychiatry, Kansai Memorial Hospital,

^bDepartment of Neuropsychiatry, Kansai Medical University, Osaka, Japan; ^cThe KEY Institute for Brain-Mind Research, University Hospital of Psychiatry, Zurich, Switzerland;

^dDepartment of Empirical and Analytical Psychophysics, Institute for Frontier Areas of Psychology and Psychohygiene, Freiburg i.Br., Germany; ^eDepartment of Neurology, Kansai Medical University, Fumizonochi Moriguchi, Osaka, Japan

Ethanol effects on 19-channel, eyes-closed EEG before and twice during ethanol (50 ml (40 mg) diluted with 450 ml saline) and control infusion (500 ml saline), reversed sequence in half the subjects, were studied in eight male, right-handed, aldehyde-dehydrogenase-2 homozygous normal subjects (24.0 ± 0.7 years). Thirty seconds of EEG per subject and condition were analyzed using space-oriented approaches. Ethanol serum concentrations after 20 and 40 mg infusion reached 0.45 ± 0.12 and $0.75 \pm$

0.12 mg/ml (drunkenness level), respectively. Significant results included the following: absolute Global Field Power (aGFP) during 40 mg ethanol infusion increased from both baseline and saline in the delta frequency band (1.5–6 Hz), but decreased in beta3 (21.5–30 Hz). Also, relative Global Field Power (rGFP) during 20 mg ethanol decreased in beta3, and during 40mg ethanol decreased in alpha2 (10.5–12 Hz), beta1 (12.5–18 Hz), beta2 (18.5–21 Hz) and beta3. Consistent with these findings, centroid values of GFP frequency spectra and the global index 'Phi' (generalized frequency) decreased during 40 mg ethanol. LORETA specified that 40 mg ethanol compared to baseline as well as saline maximally increased delta in left Brodmann areas (BA) 18, 37 and 40 and mesial BA 19, and alpha1 (8.5–10 Hz) in mesial BA 29. LORETA with subject-wise normalization specified that compared to saline, 20 mg ethanol maximally reduced beta1 in mesial BA 24, and 40 mg ethanol maximally reduced alpha2 in left BA 1, 2, 3, 6, 13 and 36, in mesial BA 6 and 24, and in right BA 37, beta1 in mesial BA 24 and in right BA 6, beta2 in mesial BA 25, and beta3 in mesial BA 24 and in right BA 6, 11 and 24. Further, Global Dimensional Complexity decreased during 40mg ethanol. These results reflect inhibitory effects of ethanol on the brain, especially around the limbic area and in occipital cortex.

S5-2

Naive EEG and Treatment Effects in Neuroleptic-Naive Schizophrenic Patients: Omega Complexity and Local Complexity Differentials

Mitsuru Kikuchi^b, Thomas Koenig^a, Yuji Wada^c, Masato Higashima^b, Tatsuya Nagasawa^b, Masafumi Yoshimura^d, Yoshifumi Koshino^b, Werner Strik^a, Thomas Dierks^a

^aUniversity Hospital of Clinical Psychiatry, Department of Psychiatric Neurophysiology, Bern, Switzerland; ^bDepartment of Psychiatry and Neurobiology, Graduate School of Medical Science, Kanazawa University, Kanazawa, ^cDepartment of Psychiatry, Fukui University, Fukui, ^dDepartment of Psychiatry, Kansai Medical University, Osaka, Japan

Brain coordination or complexity could be assessed by EEG Omega complexity analysis. Previous studies reported the increased global Omega complexity in patients with schizophrenia, which imply the impaired neuronal cooperation in various large-scale neural networks in schizophrenia. The main purpose of this study is to investigate the drug treatment effect on Omega complexity. In addition, topographical differences were also compared using a new method, local complexity differentials (LCD), i.e., virtual variations of Omega-complexity caused by exclusion of each electrode (Wackermann, 2002). EEG analysis was performed in 21 drug-naive patients, 21 healthy controls, and in 14 patients after psychoactive drug administration. Same as previous studies, drug-naive patients showed higher global Omega complexity. Analysis of LCD demonstrated that activities in frontal area tended to contribute to high global Omega complexity in schizophrenia. As a treatment effect, although there was no significant difference between before and after treatment, significant difference was observed between responder and non-re-

sponder. In addition, change of global Omega complexity was correlated with improvement of schizophrenic symptomatology. Correlation maps between change of LCD and that of schizophrenic symptomatology showed higher positive correlation in left frontal area. These results imply that, although high global Omega complexities seem to be trait marker in patients with schizophrenia, decrease in contribution of frontal area to global complexity after treatment may reflect somewhat beneficial effect of drug medication in schizophrenia.

S5-3

How Levodopa Influence to Enlarged P3 Amplitude of Non-Demented de novo Parkinson's Disease?

H. Tanaka, Y. Watanabe, T. Ogawa, A. Hozumi, K. Hirata

Department of Neurology, Dokkyo Medical University, Tochigi, Japan

Background: Some investigators reported enlarged P3 amplitude in non-demented Parkinson's disease patients (PDPs). The loss of dopaminergic neurons which is the main neuropathological cause of the disease might trigger this phenomenon resulted in the lack of habituation. **Aim:** To evaluate the habituation effect, we investigated the difference of P3 components between 1st and 2nd session. In addition, the influence of levodopa to the P3 components in de novo PDPs was assessed. **Subjects:** We studied 30 PDPs and 30 age-, sex- and education-matched normal controls (NCs). All PDPs had never received anti parkinsonian drugs and 12 patients of them administered levodopa plus benserazide for daily 300 mg. **Methods:** Event-related potential (ERP) with auditory oddball P3 paradigm and neuropsychological test batteries were recorded from all subjects, and before and after medication of 12 patients. The PDPs assessed the duration of illness and the severity with Unified Parkinson's Disease Rating Scale (UPDRS). For the ERP components, reference-independent measures (global field power = GFP) were determined in addition to conventional Fz, Cz, Pz observations, and the P3 peak amplitude and latency were measured. In addition, we investigated the difference of P3 components between 1st and 2nd session to evaluate habituation effect. And the electrical source was determined by low resolution brain electromagnetic tomography (LORETA). **Results:** Enlarged GFP P3 amplitude was confirmed in PDPs. The GFP P3 amplitude of 2nd session was significantly attenuated in NCs, but not in PDPs. The habituation effect assessed by the difference 1st and 2nd session of the GFP P3 amplitude negatively correlated with the duration of illness and UPDRS score. LORETA of the GFP P3 revealed hyperactivities of superior temporal lobe although the Fz P3 decreased activities of prefrontal lobe in PDPs compared with NCs, and the identical GFP P3 activities were observed in the 1st session compared with its 2nd session of NCs. After administration of levodopa, the GFP P3 amplitude attenuated and the attenuation effect was only shown in the group of early duration of illness within 1 year. **Conclusions:** The increased GFP P3 amplitude was caused by lack of attenuation at the 2nd session and it may reflect the habituation (set-shifting) deficits in PDPs. And the superior temporal lobe hyperactivities may reflect the lack of habituation caused by dysfunction of prefrontal

lobe. Levodopa decrease the P3 amplitude resulted in the affect to neural circuit connecting frontal cortex with the striatum and normalize its function.

S5-4

Antipsychotic Single Oral Administration as Predictor of Response to Pharmacotherapy: EEG Changes in High Schizotypal Scored Healthy Volunteers

M.J. Barbanj^a, E. Grasa^a, S. Clos^a, S. Romero^b, M. Yritiar^a, V. Perez^c

^aCentre d'Investigació de Medicaments, HSCSP, Departament de Farmacologia i Terapèutica, UAB, ^bCentre de Recerca en Enginyeria Biomèdica, UPC, ^cServei de Psiquiatria, HSCSP, Barcelona, Spain

Objective: Provide empirical support to the 'test dose procedure' and EEG changes as possible predictors of clinical response in schizophrenia integrating 3 aspects: a) plasma concentrations, b) atypical antipsychotics and c) experimental strategy using a genetically linked group. **Methods:** Single oral administration of haloperidol 3 mg, risperidone 1mg, olanzapine 5mg and placebo following a double-blind, cross-over design. EEGs and plasma concentrations were assessed before and at several times after drug ingestion in 2 groups of volunteers: a) healthy/normals to describe and quantify characteristic EEG changes, b) healthy but with O-LIFE scores >1 SD from the mean. EEG variables were computed as means of 19 electrodes after spectral analysis. Drug specific EEG pattern of changes was derived from the difference between post-drug changes and post-placebo changes [average of 4 recording times integrating time period with highest plasma concentrations (+4, +5, +6, +7 h) in relation to the average of 2 recording times pre-drug intake]. Those differences significantly different from 0 (t test, $p < 0.05$, bilateral) defined the characteristic vector of changes for a particular drug. An individual subject was classified as non-presenting the characteristic pattern of changes if $\geq 50\%$ of vector variables had a value $> 1\text{SEM}$ in the opposite direction to the one stated as characteristic. **Results:** Samples were composed by 20 healthy normals (20.3 mean O-LIFE score) and 9 healthy schizotypals (61.7 mean O-LIFE score). The probability of non-presenting the described as characteristic pattern of changes was significantly higher in the schizotypal group (3 out of 27) than in the normal group (0 out of 60) [Fisher test: $p = 0.028$]. However, the probability that one variable within the vectors had a value $> 1\text{SEM}$ in the opposite direction to the one stated as characteristic was not different between groups (schizotypals 10.9% vs normals 11.3%). **Conclusions:** These results provide additional empirical evidence to consider the 'test dose procedure' and EEG changes as possible predictors of clinical response in schizophrenia.

Supported by: Grant from the Fundació La Marató de TV3 (Catalonian Television, Spain).

Double-Blind, Placebo-Controlled, Multiple-Ascending-Dose Study on the Pharmacodynamics of Abio-08/01. A New CNS Drug with Potential Anxiolytic Activity: EEG-Mapping/Loreta (Low-Resolution Brain Electromagnetic Tomography), Psychometric and Tolerability Findings

B. Saletu^a, P. Anderer^a, M. Wolzt^b, H.V. Semlitsch^a, D. Nosiska^a, A. Assandri^c, P. Nessi^c, F. Nannipieri^d, G.M. Saletu-Zyhlarz^a

Departments of ^aPsychiatry, ^bClinical Pharmacology, Medical University of Vienna, Vienna, Austria;

^cCross S.A. – Cross Research S.A., Arzo, Switzerland;

^dAbiogen Pharma S.p.A., Pisa, Italy

Background/Objectives: In a double-blind, placebo-controlled, multiple-ascending-dose study, the pharmacodynamics of ABIO-08/01, a new potentially anxiolytic isoxazoline, were studied by pharmaco-EEG and psychometry. **Materials and Methods:** 16 young healthy males received 3 oral doses (10, 20, 40 mg) and placebo for 7 days (wash-out: 8 days). Evaluations were done at the h 0, 1 and 6 of day 1 (acute effect) and day 5 (sub-acute/superimposed effect). A 3-min vigilance-controlled EEG (V-EEG), 4-min resting EEG (R-EEG) and a 1-min eyes-open EEG (EO-EEG) were recorded. Psychometry comprised attention, concentration, memory, complex reaction time, fine motor activity and mood. Pulse rate, blood pressure and tolerability were monitored, too. **Results:** MANOVA/Hotelling T² test of Q-EEG showed significant acute, subacute and superimposed central effects of all 3 doses of ABIO-08/01 vs. placebo in all 3 recording conditions. Univariate analysis revealed activating patterns in the R-EEG (decrease in δ , θ , β ; increase in α -2; acceleration of the total centroid (TC)), with a positive dose-efficacy relation (40, >20, >10 mg). In the EO-EEG, sedative (relaxing) patterns occurred (increase in δ , θ ; decrease in α , slowing of TC), with a negative dose-efficacy relationship (10, >20, >40 mg). In the V-EEG, 40 mg induced activation, 10 mg sedation. LORETA identified target regions of the drug. Psychometrically, the ABIO-08/01 improved concentration dose-dependently (40, >20, >10 mg) (activation) and decreased mood inverse-dose-dependently (10, >20, >40 mg) (sedation). 10 mg also improved reaction time performance and psychomotor activity. The dose-dependent increase in reaction time is due to a sequence effect. The drug was well-tolerated. **Conclusion:** ABIO-08/01 may be of therapeutic benefit in neurotic and stress-related disorders.

Session 6: Neuro-Imaging in Psychiatry

New Techniques of Neuroimaging

Tetsuo Kobayashi

Graduate School of Engineering, Kyoto University, Kyoto, Japan

Background/Objectives: What is consciousness? What mechanisms in the brain are associated with mind? An important step to answer these questions is obtaining knowledge about dynamic processes underlying certain brain activities such as perceptions, cognitive behaviors. Although recent neuroimaging techniques, such as fMRI, MEG and NIRS, have become powerful tools for exploring the higher brain functions, each technique still has the limitation of spatial and/or temporal resolutions that hamper our understanding of dynamic brain processes. To reveal the dynamic processes, we have been investigating new techniques of neuroimaging. Here, we introduce a newly developed fMRI-MEG integrative source localization technique. **Materials and Methods:** Procedures of the present technique were consisted with some sequential steps. Firstly, activated cortical regions were determined by the statistical analysis of fMRI data. Secondly, the orientations of equivalent current dipoles placed at individual activated regions were estimated by a procedure maximizing inner product of lead field and measurement field vectors. The time-varying dipole moments were obtained by the projection of the optimized lead field vector to measured fields. We applied the technique to data obtained during a visual perception task. An apparent motion stimulus, which activates multiple cortical areas simultaneously, was used in the experiments. Event-related neuromagnetic fields were obtained by a 306-channel MEG system (Elekta Neuromag), whereas fMRI data were acquired by a 1.5-T MR system (Siemens, Sonata). Seven healthy subjects with normal and corrected-to-normal visual acuity participated in the experiments. **Results:** Although there were individual differences, the present fMRI-MEG integrative source localization technique successfully detected dynamic neural activities in multiple visual areas including the parietal association area, such as V1, V2, V5 and IPS. The results demonstrate that the present integrative technique is promising for revealing dynamics of multiple distributed cortical activities. **Conclusion:** The availability of new neuroimaging techniques with high spatio-temporal resolution would provide important advancements in cognitive brain research, and improve clinical diagnosis and management of neurological and psychiatric disorders.

S6-2**An EEG Symptom Provocation Study in Patients with Obsessive Compulsive Disorder**

M. Yoshimura^{a, b}, T. Koenig^b, Y. Saito^a, K. Nobuhara^a,
T. Isotani^{a, c}, M. Kikuchi^{b, d}, G. Okugawa^a, S. Irisawa^a,
K. Yamada^a, T. Kinoshita^a, W.K. Strik^b, T. Dierks^b

^aDepartment of Neuropsychiatry, Kansai Medical University, Osaka, Japan; ^bDepartment of Psychiatric Neurophysiology, University Hospital of Clinical Psychiatry, Bern, Switzerland;

^cDepartment of Psychiatry, Kansai Memorial Hospital, Osaka,

^dDepartment of Psychiatry and Neurobiology, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan

Aim: To investigate changes on brain electric field induced by anxiety provocation in patients with obsessive compulsive disorder (OCD). **Methods:** Nine OCD subjects who had contamination fear participated in this study. Nineteen-channel spontaneous EEGs were recorded at four occasions for each subject; before and after symptom provocation (pre and post condition, respectively), clean control condition (control) and during imaginative exposure for what subjects feared (exposure). EEG microstate analysis with four classes (A, B, C and D) and Low resolution brain electromagnetic tomography (LORETA) were applied to analysis. **Results:** We found that exposure changed microstate configurations of class A, B and C. Then, the microstate configurations normalized in the post condition. LORETA revealed decrease of current density during exposure at right lateral orbitofrontal, lateral frontal, anterior medial temporal, and limbic area in theta band, and at right inferior frontal, anterior lateral temporal, and limbic area in alpha2 band. **Conclusions:** The changes of microstate configurations suggest that they are state dependent. The decrease of current density in theta and alpha band can be interpreted as activation of brain function. Therefore, we conclude that the symptom provocation induced alterations of the neuronal activity pattern and that the results presented were similar to the results of previous symptom provocation studies in OCD patients. We think that we should perform a control study with provocation in healthy subjects to investigate possible trait effects.

S6-3**QEEG Subtyping and Source Localization Reveal the Need for Polypharmacy**

E. Roy John, Leslie S. Prichep, Robert Cancro

Brain Research Laboratories, Department of Psychiatry,
New York University School of Medicine and Nathan Kline
Psychiatric Research Institute of New York State,
New York, N.Y., USA

Neurometric QEEG analysis was performed on a group of 390 patients comprised of 228 who were diagnosed using ICD-10 as schizophrenic, 134 as depressive psychosis, and 28 as alcoholic psychosis. Using cluster analysis based on only QEEG variables, six subtypes were identified, replicating results previously ob-

tained in a group of 134 patients all diagnosed as schizophrenic using DSM-4. Variable Resolution Electromagnetic Tomography (VARETA) was then used to localize the sources within the brain of the most excessive and most deficient QEEG activity in the Z-spectra of each subtype. The images thereby obtained revealed that one set of neuroanatomical regions was uniformly depressed in each subtype, implying a common down-regulation of some neurotransmitter in all of the psychotic patients. However, a second quite different set of brain regions was differentially overactive, implicating a unique neurochemical up-regulation in every subtype. These results, yielded by combining QEEG, cluster analysis, and source localization, suggest that optimum treatment of psychotic patients irrespective of the formal clinical diagnosis, will require the administration of both an inhibitory and an excitatory agent.

S6-4**Association between Functional and Structural Deficits in Brain Regions Subserving Face Processing**

Toshiaki Onitsuka^{a, b}, Margaret A. Niznikiewicz^b,
Robert W. McCarley^a

^aDepartment of Neuropsychiatry, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan;

^bClinical Neuroscience Division, Laboratory of Neuroscience, Department of Psychiatry, Boston VA Healthcare System, Brockton Division and Harvard Medical School, Brockton, Mass., USA

Background: Schizophrenia impairs many cognitive functions, including face perception. Veridical face perception is critical for social interactions, and for distinguishing friend from foe, and familiar from unfamiliar faces. However, it has remained unclear which aspects of face perception are abnormal in schizophrenia, and what are the mediating brain regions. **Aim:** To determine whether or not patients with schizophrenia show less activation in neural networks related to face processing than healthy subjects, and to investigate relationships between this functional abnormality and magnetic resonance imaging (MRI) anatomical abnormalities in the fusiform gyrus (FG). **Methods:** Twenty male chronic schizophrenia patients and 16 age-, gender-, handedness-, and parental socioeconomic status-matched normal controls underwent high-spatial-resolution MRI; Event-related potentials were recorded to faces, cars and hands in a separate session. **Results:** Schizophrenia patients, relative to controls, showed bilateral N170 reduction to faces but not to other objects. Patients also showed bilateral anterior and posterior FG gray matter volume reduction (10%). In addition, the right posterior FG volume was significantly correlated with N170 to faces at the right posterior temporal electrode ($r = -0.69$ at P8) in patients with schizophrenia, but not in normal controls. **Conclusion:** These results provide evidence for deficits in the early stages of face processing in schizophrenia, whose association with FG volume reduction points to the site of a defective anatomical substrate for face processing.

S6-5

Neuroimaging in Dementia

T. Dierks

Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, Bern, Switzerland

Dementia is characterized by neuronal degeneration, which affects cerebral regions differentially. This degeneration leads to typical spatial patterns of electrophysiological and consequently in metabolic pattern both during resting and cognitive activation. These patterns can be investigated by neurophysiological and other imaging techniques (e.g. SPET, PET, MRI). The pathophysiology of cognitive dysfunction can be assessed by e.g. EEG and functional MRI (fMRI). Resting EEG alterations reported are mostly a general slowing, increase in especially theta and decrease in alpha and beta activity, and alterations of the spatial EEG pattern, which is related to the disturbed metabolic pattern of glucose metabolism assessed by PET. Both electrophysiological as well as metabolic indices have been suggested to be well suited to predict a dementive development in clinical healthy elderly subjects and in subjects with Mild Cognitive Impairment (MCI). Functional MRI can assess the relation between behavior, neuronal activity and anatomical structures. EEG data during the development of cognitive impairment will be presented together with possible influence on electrical brain activity by drug therapy. Furthermore a pathophysiological model of task demand dependent alterations of cerebral blood flow (BOLD-fMRI) during visuospatial processing in late life and in increasingly severe cognitive disturbance will be presented and discussed from a diagnostic, predictive and therapeutic standpoint.

S6-6

Microstate Analysis of Neuroleptic-Naïve Schizophrenic Patients

Toshihiko Kinoshita, Satoshi Irisawa, Toshiaki Isotani, Takami Yagyu, Sachi Tsukamoto, Keiichiro Nishida, Masafumi Yoshimura Gaku Okugawa, Kenji Nobuhara

Department of Neuropsychiatry, Kansai Medical University, Osaka, Japan

The pathophysiology of schizophrenia is unclear, although many researchers in psychiatry and related fields have endeavored to elucidate the etiology. Up to date neuroimaging techniques such as functional magnetic resonance imaging (fMRI), single photon emission computed tomography (SPECT), diffusion tensor imaging (DTI) and positron emission tomography (PET) have revealed various degrees of degraded connectivity in patients with schizophrenia. The aims of the present study was to explore degraded brain connectivity and altered brain information processing in schizophrenic patients, EEG microstate analysis was applied for 24 neuroleptic-naïve untreated patients and 24 healthy subjects. Three topographical classes were obtained from all EEG data by microstate analysis. Microstate analysis makes it possible to detect that the momentary brain state is reflected directly by the momentary spatial configuration of the brain elec-

tric field., and changes of brain electric field configuration can only be caused by changes of the active neural elements, and such changes most probably imply changes of the brain function. The mean duration of one topographical class in the patients was shortened compared to healthy subjects. These results indicated looser cooperativity, or decreased connectivity of active brain function and deviant brain information processing in schizophrenic patients.

Session 7: Past, Present and Future of Pharmaco-EEG as a Biomarker

S7-1

Introduction – The History of the IPEG and of Pharmaco-EEG as a Predictive Biomarker of Drug Effects

Gé S.F. Ruigt

NV Organon, Oss, The Netherlands

The history of the evaluation of the central effects of psychotropic drugs by means of EEG dates back to the early days, when Berger discovered the human EEG and described its modulation by cocaine, which was followed by many descriptive drug-EEG studies in the forties and fifties. But the real dawn of pharmaco-EEG was linked to the impact which the discovery of antidepressants and antipsychotics had in psychiatry, the advances in EEG instrumentation and computational techniques, and the finding that compounds with similar therapeutic action had similar human EEG profiles, making EEG a putative predictive biomarker for their psychotherapeutic potential, which was embraced by the pharmaceutical industry and by pharmaco-psychiatry alike, leading to the foundation of the IPEG and a surge in p-EEG studies in the drug development process during the sixties and the seventies. This enthusiasm abated in the eighties and nineties with the developing focus within the industry on molecular pharmacology at the expense of in vivo behaviour, with the limitations of therapeutic predictions made for compounds with novel mechanisms of action, and with the rise of novel techniques providing more imaginative windows into the brain. The last decade, however, has generated exciting data, e.g. on multi-lead p-EEG tracings allowing EEG brain imaging, on multimodal recordings combining high spatial resolution imaging with high temporal resolution EEG, and on PK-PD modelling of p-EEG effects enabling resolution of the molecular characteristics of drug action in man in vivo, which combined with hardware and software progress in EEG recording and analysis should bring EEG back into the mainstream of drug development and drug discovery in the current era, in which translational medicine and the need for biomarkers are of prime importance. This symposium is meant to reemphasize these potential opportunities of p-EEG not in contradistinction but in combination with other brain research methods.

S7-2

High Resolution Functional Imaging with EEG – A Biomarker of Central Drug Effects

Roberto D. Pascual-Marqui

The KEY Institute for Brain-Mind Research, University Hospital of Psychiatry, Zurich, Switzerland

The field of Pharmacology-EEG has seen great developments in recent years. At the basis of this area of science lies the simple, but fundamental fact that centrally active medications yield reproducible quantitative changes in EEG activity. From a simplistic methodological point of view, the quantification of drug-induced EEG changes has evolved through three major steps: (1) The use of single-electrode power spectral features. (2) The use of scalp map features for multichannel recordings. (3) The use of source localization methods, i.e. functional mapping of electrically active neuronal populations. This work presents an overview of the method known as low resolution brain electromagnetic tomography (LORETA), which has been used in a number of Pharmacology-EEG studies. Emphasis is placed on the electrophysiological and neuroanatomical basis of the method: scalp electric potentials (EEG) are generated by the primary current density distribution that arises from highly synchronized neuronal post-synaptic processes. The localization properties of LORETA, and its validation based on real experimental human data are reviewed. Methods for going beyond localization towards central drug effects on intracortical connectivity are introduced.

S7-3

Translational Value of Pharmacology-EEG: Extrapolations from Animal to Man and vice versa

W.H.I.M. Drinkenburg, A. Ahnaou

CNS Biomonitoring Center of Expertise, Johnson & Johnson Pharmaceutical Research and Development, RED Europe, Beerse, Belgium

Introduction: While the study of animal EEG dates back to the pioneers of EEG over 130 years ago, still the animal EEG and even more so the animal pharmacologyEEG remains enigmatic in many of its complex aspects. This complexity has not prevented researchers all over the world to study in animals the relationship between psychoactive pharmacological agents and their concomitant cortical electrical brain waves. Furthermore, a broad arsenal of recording and analysis techniques has been developed since the pioneering days and contemporary animal EEG scientists usually quickly embrace new tools. Nevertheless it is fair to state that the use of animal pEEG has seen some peaks and troughs in popularity over time. More recently the popularity of animal pEEG seems to increase once again, probably partly driven by the high demand from pharmaceutical companies to develop and validate new biomarkers in translational science for CNS drug discovery and development: pEEG still remains one of the few techniques that can be used non-invasively both in animals and man with an unparalleled time resolution. The increasing availability of powerful visualization and analysis tools and the technical possibilities to

combine animal pEEG with other preclinical in vivo test assays (e.g. cognitive tests) further contributes to its 'revival'. An integrative behavioral EEG approach is believed crucial to facilitate translation of animal pEEG data to clinical pEEG studies in a more refined manner. **Aim/Conclusions:** The talk aims to present an up-to-date overview on the present state of use of pEEG within the field of translational medicine. Thus far several translational pEEG applications such as in PK/PD marker identification or in sleep-wake organization analysis have been used and yielded sometimes mixed, sometimes promising results. Limitations as well as advantages can be outlined in comparison to other imaging techniques such as MRI. The need for more advanced task-related pEEG protocols will be exemplified and made evident from present limitations and difficulties in interpretation of conventional pEEG recording conditions. Moreover, such an approach is fully in line with ongoing efforts to translate clinical observations back to the preclinical setting in novel animal pEEG models. Data now start to become available that should proof the added value of such translational preclinical pEEG models and justify their use in drug development based on their predictive but also on their construct validity.

S7-4

Positioning of EEG in the Present Biomarker Area of Drug Development

R. Luthringer, C. Gilles

FORENAP Pharma, Rouffach, France

While the role of qEEG has been largely described in the literature as a tool for psychotropic drug classification, its place as a biomarker in early clinical drug development needs to be emphasized. The primary goal of this presentation is to review the most used challenge models in healthy volunteers with a special attention to qEEG as a biomarker. First, basic statements of challenge models in healthy volunteers and indications on the way to integrate these models into adapted phase I trials are given. Then, examples of challenge studies in depression, schizophrenia and cognitive disorders conducted in our facilities are presented with the aim to better characterize the advantages and drawbacks of qEEG compared to rating instruments and other functional markers in the decision to pursue with further development of the candidate drug.

S7-5

QEEG as an Adjunct to Diagnosis and a Monitoring Tool for Psychiatric Dysfunction – The Evolution of Dementia in the Elderly

L.S. Prichet^{a, b}, E.R. John^{a, b}

^aBrain Research Laboratories, Department of Psychiatry, NYU School of Medicine, New York, N.Y., ^bNathan S. Kline Institute for Psychiatric Research, Orangeburg, N.Y., USA

The clinical utility of the EEG as an adjunct to diagnosis, especially in psychiatric, learning and cognitive disorders, has been

greatly enhanced by the use of quantitative analysis (QEEG) and comparisons to a normative database. A recent meta-analysis of the clinical significance of this approach spanning over 20 years, attests to the fact that QEEG provides high sensitivity and specificity to abnormalities in brain function seen in neuropsychiatric populations. Clinical utility is further aided by the use of QEEG to subtype within disorders with homogeneous clinical presentations. Subtypes have to demonstrated to have differential pharmacological treatment responses in many disorders, including obsessive compulsive disorder, attention deficit disorder, depression and others. Additionally, taking advantage of the very high test-retest reliability of QEEG values in the absence of intervention, it may be possible to objectively assess the bioavailability of a pharmacological intervention by statistical indication of normalization of the QEEG values in test and retest comparison after an appropriate interval. High sensitivity to functional abnormalities of the brain allow assessment of disorders not seen by other neuroimaging tools. A study demonstrating prediction of evolution of dementia will be described in this presentation. **Subjects and Methods:** Forty-four subjects were studied (22M/22F, with a mean age of 72 years.). All subjects were staged using the Global Deterioration Scale as GDS 2's, i.e., normal elderly with only subjective complaints about memory. Subjects were electrophysiologically evaluated (baseline) and were then followed for 5–7 years with clinically/cognitively re-staging of GDS at intervals during this time period. Retrospectively, subjects were divided into those who showed no decline throughout the follow-up period (remaining at GDS stage 2) and those who declined to MCI or AD (changed to GDS Stage 3 or higher). Two minutes of artifact-free data were selected for analysis from a 20 min eyes closed resting EEG recording, from 19 lead recordings referenced to linked ears. Quantitative features were extracted, log transformed, age-regressed, and Z-transformed relative to age appropriate population norms for the standard wide frequency bands. In addition, using norms for narrow band spectral power, Z transformed spectra were computed. Variable Resolution Electromagnetic Tomography (VARETA) was used to identify the most probable underlying sources from the scalp recorded EEG at the maxima of the Z-spectra in the theta range. **Results:** Using selected features from only the baseline QEEG evaluations, significant differences were found between 'Non-Decliners' and 'Decliners,' [F(12,31) = 5.08, $p < 0.0001$]. Decliners were then further divided into those who declined to MCI and those who converted to AD and compared to those subjects who did not decline. Using a logistic regression, the overall prediction accuracy was 90%, with an R^2 of 0.93, $p < 0.0001$. Considering only those who in fact converted to dementia (GDS ≥ 4), the sensitivity was 96.3% and the specificity was 94.1% and considering only those who decline to MCI, the sensitivity was 95% and specificity was 94.1%. Contributing maximally to the regression were absolute power across all frequency bands diffusely on the right hemisphere, especially on the right dorsolateral frontal region, increased in decliners and greatly increased in converters; and absolute power in the theta frequency band across the right frontal regions, greatly increased in decliners. Clear differences between the groups were seen in the VARETA images, with successively more regions of abnormality and involvement of additional regions of interest in those groups who go on to show decline in the future, with increasingly significant abnormalities seen in the hippocampus, parahippocampal gyrus, amygdala and parieto-

temporal cortex, were seen in the *Converters* as compared with *Decliners*. **Conclusions:** One of the critical factors contributing to the sensitivity demonstrated in this and other studies is the existence of norms for the QEEG measures and sources, across the human life span. Abnormalities can thus be identified and quantified as statistical deviations from age expected normal values. The abnormalities reported in this study in the BL QEEG of normal elderly who go on to decline to MCI or convert to dementia demonstrate sensitivity of QEEG to the earliest manifestations of subcortical as well as cortical changes. QEEG with source localization may represent a, non-invasive brain imaging tool capable of identifying the earliest signs of brain dysfunction in subjects with evolving MCI or dementia and help in monitoring interventions in other neuropsychiatric disorders.

S7-6

The Q-EEG as a Biomarker – From EEG Fingerprinting to the Key-Lock Principle

B. Saletu

Department of Psychiatry, Medical University of Vienna, Vienna, Austria

Following the early observation of Berger (1933) that drugs altered the human EEG, these effects were studied by visual evaluation in over 600 reports between 1951 and 1963 (Fink 1964). Drugs with similar EEG effects seem to have similar clinical effects. The introduction of computer-assisted quantitative analysis of single-lead recordings in combination with statistical procedures ('pharmac-EEG') between 1960 and 1970, and from the 1980s onwards of multi-lead analysis and subsequent mapping techniques came just in time for the quickly developing area of psychopharmacology. It became possible to objectively and quantitatively determine if, how, when and at which dose a compound is CNS-effective as compared with placebo. The main psychopharmacological classes, such as sedative and non-sedative neuroleptics and antidepressants, tranquilizers, hypnotics, psychostimulants and cognition-enhancing drugs, induced typical EEG profiles and maps. On the other hand, different mental disorders, such as positive and negative schizophrenia, major depression, generalized anxiety disorder, agoraphobia, obsessive-compulsive disorder, multi-infarct dementia, senile dementia of the Alzheimer type, and alcohol dependence, showed EEG maps that differed from those of normal controls and from each other. In many instances, these differences were opposite to those between psychotropic drugs and placebo in normal volunteers. Thus, it seems possible to choose the optimum drug for a specific patient according to a key-lock principle, since the drug should normalize the deviant brain function. This is also supported by the latest advances in the Q-EEG – EEG topography such as low-resolution brain electromagnetic topography (LORETA), which identifies brain regions affected by psychiatric disorders and psychopharmacological substances.

Session 8: Aroma

S8-1

Odor Effects on Vigilance

Miyuki Matsumura, Mikio Osawa, Makoto Iwata

Department of Neurology, Tokyo Women's Medical University, Tokyo, Japan

Background: Some kinds of odor are thought to be effective in raising the vigilance level. The Pb component of mid-latency auditory evoked potentials (MLRs) is postulated to be generated in cholinergic neurons of the ascending reticular activating system. The vigilance level was evaluated based on the enlargement of Pb in an active perceptual cognitive task as compared to that in a passive listening task. We investigated effects of odor on vigilance using Pb. **Materials and Methods:** The subjects comprised ten healthy volunteers, six men and four women, aged 23–35 years (mean: 27). In a passive listening task, pure tones of 1,000 and 2,000 Hz, respectively, were binaurally presented via headphones. In an active perceptual cognitive task, 1,000 and 2,000 Hz pure tones were given in a random sequence, each occurring 50% of the time. The subjects were instructed to mentally count the number of times they heard the 2,000 Hz tone which was designed as a target stimulus. MLRs were recorded from 15 electrodes on the scalp, referred to the tip of the nose, and in each task, two blocks, each consisting of 125 artifact-free trials, were averaged off-line. The subjects were instructed to take a seat with their eyes open. Topographical mapping (TM) was drawn based on the peak amplitude of Pb at 15 recording sites. We used odor of lemon, mint and coffee one at a session. MLRs were recorded before, during and after its inhalation. **Results:** On TM, Pb, which was distributed dominantly in Cz, showed enlargement in an active perceptual cognitive task as compared to that in a passive listening task. This enlargement was not changed by the odor of lemon or coffee, but was enhanced by that of mint. **Conclusion:** The above mentioned results suggest that the vigilance level is raised by the odor of mint, but not by that of lemon or coffee.

S8-2

Olfactory Cognitive Responses Measured by EEG and MEG

Mitsuo Tonoike^a, Fumikazu Miwakeichi^a, Masahiko Yamaguchi^b, Koichi Sutani^b

^aDepartment of Medical System Engineering, Chiba University, Chiba, ^bKansai Center, Humanbiomed, National Institute of AIST, Ikeda, Japan

Background/Objectives: Although the sense of olfaction is important in our daily lives, the mechanism of olfactory recognition is still unknown now. The aim of this study is to measure and analyze perception and cognition in human olfaction using objective and non-invasive techniques. In this study, the event-

related potentials and magnetic fields were measured by electroencephalography (EEG) and magnetoencephalography (MEG) using a multi electrode system and a whole cortex bio-magnetometer. **Materials and Methods:** In this MEG experiments, we used following two methods to measure olfactory cognitive responses. The first experiment is olfactory EEG and MEG measurements of the odd-ball paradigm using two kind odorants (for example: amyl acetate, good odor like 'banana', and iso-valeric acid, bad odor like 'sweat'). This experimental method was a passive olfaction using a blast method. The subjects were instructed to count the number of rare odor stimulation as a target. The second experiment of olfactory cognitive test is the measurement of an active olfaction using a sniffing method of odor. In this sniffing experiment, the subjects were instructed active sniffing odor by themselves. We used a special mask to the subjects sniffing the odor. **Results:** In the first MEG experiment, we have analyzed to apply a SSP (signal space projection method) which is one of the special methods in PCA (principal component analysis). From this SSP analysis for our data of the olfactory odd-ball paradigm, an olfactory cognitive later response was obtained which had the latency about 500ms, and estimated at superior-temporal area. In the second MEG experiment, as a prepared moving response was included in these sniffing data, the SSP method was again applied to reject the prepared moving response related with a sniffing action, and a pure olfactory response was only obtained from our olfactory sniffing data. The source of this analyzed sniffing response was estimated at a right frontal area only. **Conclusion:** These above two olfactory cognitive responses gave us the different results and the different estimated areas for olfactory cognitive activities. This difference may be considered as the result of a capability of different olfactory cognitive mechanism between a passive and an active olfaction.

S8-3

Hypnotic and Sedative Effects of Santalol

T. Nakajima^a, Y. Koga^a, Y. Hasegawa^b, M. Kawasaki^b

^aDepartment of Neuropsychiatry, Kyorin University School of Medicine, ^bKobayashi Pharmaceutical Co., Ltd., Tokyo, Japan

Objective: Essential oil derived from sandalwood has been used for aromatherapy aimed at alleviating various symptoms. Its major component, santalol, has been reported to suppress the central nervous system in rats, exerting sedative and other effects. The present study was undertaken to evaluate the hypnotic and sedative effects of santalol in 12 healthy volunteers of both sexes. **Methods:** The subjects of this study were 12 individuals (6 males and 6 females aged between 20 and 23 years) who satisfied all of the following requirements: (1) having given informed consent to the study in writing, (2) taking no medication on a regular basis, (3) no history of chronic disease, (4) nonsmokers and (5) having no habit of taking a midday nap. After approval by the ethics committee, the subjects were exposed to vapor of santalol (purity 98%) or lavender essential oil at a concentration of 5×10^{-4} ppm. Vaporized water served as control. In view of the 'day of the week effect', the first night was deemed as the night for acclimation, with no sample presented. The second to fourth nights were deemed as the test nights, during which the above three types of

vapor were presented (one vapor each day), taking the 'stimulus order effect' into account. The sample was evaporated indoors during the period from 10:00 p.m. (one hour before the bedtime) to 7:00 a.m. (immediately before getting up from the bed). The amount of activity during sleep and wake was serially measured every minute, using an Actigraph (AMI). **Results:** Analysis of variance revealed significant inter-sample differences in terms of the principal effect on the amount of activity during the falling asleep phase and the main sleep phase. The activity was smallest during exposure to santalol vapor. The percentage of the amount of stratified activities on the day following exposure to santalol

showed a significant difference. That is, the percentage of low-level activities (60–100 mG) increased and the percentage of high-level activities (220–270 mG) decreased following exposure to santalol, as compared to those after exposure to lavender or water vapor. **Discussion:** The reduction in activities during sleep and the day following exposure to santalol suggests that santalol has hypnotic and sedative effects on healthy males and females. In the present study, involving continued exposure to santalol, from bedtime to immediately before getting up in the morning, the results suggest that the pharmacological activity of santalol remains to be seen until midday or later.

Numbers refer to abstract numbers

- Ahnaou, A. S7-3
 Akiyama, T. S4-2
 Alain, C. S3-1
 Alper, K. S4-1
 Anderer, P. S1-4, S2-1, S5-5
 Asai, R. S3-2
 Assandri, A. S5-5
 Azechi, M. S4-4
- Barbanj, M.J. S5-4
 Boeijinga, P. S2-2
 Bokura, H. S3-5
- Cancro, R. S6-3
 Canuet, L. S4-4
 Clos, S. S5-4
- Dierks, T. S5-2, S6-2, S6-5
 Drinkenburg, W. S2-2
 Drinkenburg, W.H.I.M. S7-3
- Faber, P.L. S5-1
- Gianotti, L.R.R. S5-1
 Gilles, C. S7-4
 Grasa, E. S5-4
- Hara, E. S3-2
 Hasegawa, Y. S8-3
 Higashima, M. S5-2
 Hirata, K. S5-3
 Hozumi, A. S5-3
- Ikezawa, K. S4-4
 Irisawa, S. S6-2, S6-6
 Ishii, R. S4-4
 Isotani, T. S5-1, S6-2, S6-6
 Iwase, M. S4-4
 Iwata, M. S8-1
- John, E.R. S6-3, S7-5
- Kakigi, R. S3-4
 Kameda, T. S1-2
 Kaneko, S. S3-2
 Kawabata, K. S1-3, S3-6
 Kawasaki, M. S8-3
 Kemp, B. S2-1
- Kida, Y. S3-6
 Kikuchi, M. S5-2, S6-2
 Kinoshita, T. S5-1, S6-2, S6-6
 Kobayashi, T. S6-1
 Koenig, T. S5-2, S6-2
 Koga, Y. S8-3
 Kondoh, Y. S1-2
 Koshino, Y. S5-2
 Koyano, S. S1-6
 Kurimoto, R. S4-4
 Kurita, A. S1-7
 Kuroiwa, Y. S1-6
- Lehmann, D. S5-1
 Luthringer, R. S2-2, S7-4
- Maeda, T. S1-2
 Maekawa, T. S3-3
 Matsumura, M. S8-1
 Matuoka, T. S3-2
 McCarley, R.W. S6-4
 Miwakeichi, F. S8-2
- Nagasawa, T. S5-2
 Nagata, K. S1-2
 Nakajima, T. S8-3
 Nakamura, Y. S1-2
 Nakase, T. S1-2
 Nakata, H. S3-4
 Nannipieri, F. S5-5
 Nessi, P. S5-5
 Nishida, K. S6-6
 Nishimura, H. S1-3
 Niznikiewicz, M.A. S6-4
 Nobuhara, K. S6-2, S6-6
 Nosiska, D. S5-5
- Ogawa, T. S5-3
 Ogura, N. S1-2
 Oishi, M. S1-5
 Okugawa, G. S6-2, S6-6
 Onitsuka, T. S6-4
 Osawa, M. S1-8, S8-1
- Pascual-Marqui, R.D. S5-1, S7-2
 Perez, V. S5-4
 Prichep, L.S. S2-2, S4-1, S6-3, S7-5
- Robinson, S.E. S4-4
 Romero, S. S5-4
 Ruigt, G. S7-1
 Ruigt, G.S.F. S7-1
- Saito, A. S5-1
 Saito, H. S1-2
 Saito, Y. S6-2
 Saletu, B. S1-4, S5-5, S7-6
 Saletu-Zyhlarz, G.M. S1-4, S5-5
 Sato, M. S1-2
 Satoh, Y. S1-2
 Semlitsch, H.V. S1-4, S5-5
 Shinosaki, K. S4-4
 Soufflet, L. S2-2
 Strik, W. S5-2, S6-2
 Sutani, K. S8-2
- Tachibana, H. S1-3, S3-6
 Takahashi, K. S1-2
 Takeda, M. S1-3, S3-6, S4-4
 Tanaka, H. S5-3
 Tobimatsu, S. S3-3
 Toda, H. S1-6
 Tonoike, M. S8-2
 Tsukamoto, S. S6-6
- Ukai, S. S4-4
- Wackermann, J. S5-1
 Wada, Y. S5-2
 Watanabe, Y. S5-3
 Wolzt, M. S5-5
- Yabe, H. S1-1, S3-2
 Yagyu, T. S6-6
 Yamada, K. S6-2
 Yamaguchi, M. S8-2
 Yamaguchi, S. S3-5
 Yamazaki, M. S4-3
 Yamazaki, T. S1-2
 Yoshimine, T. S4-4
 Yoshimura, M. S5-2, S6-2, S6-6
 Yritiar, M. S5-4