Methods: Data were available from a sample of 40 severe MDD patients defined by DSM-IV diagnostic criteria. 19 (47.5%) men and 21 (52.5%) women, ages 17–54 years was assessed through a comprehensive clinical interview for DSM-IV Axis I Disorders and have a 17-item Hamilton Depression Rating Scale of 18 or higher. The 5-HTTLPR variant was genotyped according to published protocols. Three allele variants of the gene polymorphism were identified based on the PCR fragment sizes: short (S; 486bp, 14 repeats), long (L; 529bp, 16 repeats), or extra-long (XL; 612bp, 20 repeats).

Results: The HDRS score was 21.4 ± 2.1. The study exhibits high frequency of S/S genotype (50%), lower frequency of L/S genotype (30%), L/L genotype (17.5) and L/XL (2.5%) in severe MDD patients.

Conclusions: These results support the possibility of serotonin transporter polymorphism role in the etiology of MDD.

Key Words: Severe Major Depressive Disorder, Serotonin Transporter, SLC6A4, Indonesia

PS164
Concomitant Use of Benzodiazepine Hypnotics and Alcohol in Patients with Schizophrenia, Depression and Insomnia: A Preliminary Finding
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Abstract
Objective: Concomitant use of benzodiazepines and alcohol seems prevalent in general clinical settings; however, previous studies have not focused solely on psychiatric patients. The objectives of this study were two-fold: (1) to investigate the prevalence of concomitant use of benzodiazepine hypnotics and alcohol in outpatients with mixed psychiatric diagnoses and (2) to examine the extent of awareness on the side of their psychiatrists about the concomitant use.

Methods: A questionnaire survey was carried out for outpatients with schizophrenia, depression and primary insomnia (ICD-10) who were receiving benzodiazepine hypnotics at Kawasaki Municipal Hospital, Kanagawa, Japan. After providing informed consent, participants were asked to fill in a sleeping diary for seven days in which use of alcohol and hypnotics was also recorded, if any. In addition, their treating psychiatrists were asked as to whether or not they thought their patients were concomitant users. In total, 100 patients (mean±SD age = 54.9±13.4 years; 19 females) were included: schizophrenia (n=16), depression (n=15) and primary insomnia (n=13). The prevalence rates of concomitant use of benzodiazepine hypnotics and alcohol were 56.3% (9/16) in schizophrenia, 33.3% (5/15) in depression and 46.2% (6/13) in primary insomnia. In contrast, the rates of suspicion regarding the concomitant use by their treating psychiatrists were 55.6% (5/9), 20.0% (1/5) and 33.3% (2/6), respectively. No differences in the severity of sleep-related symptoms were observed between concomitant users and others. In participants with depression, concomitant users tended to receive more antidepressants than nonusers (Defined Daily Dose, 1.1 vs 0.7, p=0.052) although symptom severity was not significantly different.

Conclusions: Nearly half of psychiatric patients concomitantly used benzodiazepine hypnotics and alcohol, which raises a serious safety concern. Although these preliminary findings need to be confirmed by further investigations, they emphasize the need of closer attention to those hazardous combinations.

PS165
Association of cerebral amyloidosis, systolic blood pressure, and regional neuronal injury with late-life onset depression
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Abstract
Objective: Previous studies suggested that Alzheimer’s disease (AD) process may possibly contribute to late life-onset depression (LLOD). We aimed to investigate whether LLOD is associated with cerebral amyloidosis and regional cortical atrophy, the two key brain changes in AD process, considering vascular risks together.

Methods: Twenty nine non-demented individuals who first experienced major depressive episode (MDE) after age of 60 years were recruited as LLOD subjects, and 27 non-demented elderly individuals who had no life-time experience of MDE were included as normal controls (NC). All participants received a comprehensive clinical assessment including vascular risks evaluation, magnetic resonance imaging, 11C-labeled Pittsburgh Compound B (PiB) positron emission tomography and plasma beta-amyloid (Aβ) peptides level assessment.

Results: Among LLOD subjects, 48% of them had comorbid mild cognitive impairment (MCI) diagnosis, while none of NC subjects did. In VBM analysis, LLOD, irrespective of comorbid MCI diagnosis, was associated with prominent prefrontal cortical atrophy (FWE corrected p<0.05, k=100). LLOD with comorbid MCI (LLOD-MCI) subgroup showed increased cerebral PiB retention (p=0.036) and plasma Aβ1–40 (p=0.006) and Aβ1–42 peptides (p=0.03), as measures of cerebral amyloidosis, compared to NC, while overall LLOD group and LLOD without MCI (LLOD-woMCI) did not. LLOD individuals had higher systolic blood pressure (SBP) than NC subjects (p=0.017), particularly in subjects with LLOD-woMCI (p=0.026). Multiple logistic regression analysis including diagnostic group (LLOD vs. NC) as a dependent variable showed that prefrontal cortical atrophy was significantly associated with LLOD diagnostic state (p=0.002), while cerebral PiB retention and SBP did not after controlling age, gender, and education.

Conclusion: Our findings suggest that AD process probably contributes to LLOD occurrence via prefrontal neuronal injury from MCI stage, while vascular process, high SBP in particular,
is associated with LLOD in cognitively asymptomatic state via prefrontal neuronal injury.

**PS166**

Relationship of Hippocampal asymmetry and cognitive function in first-episode drug naïve major depressive disorder

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**Abstract**

It has been reported that abnormalities of functional brain asymmetry was detected in patients with major depressive disorder (MDD). However, little is known about their clinical implication. The aim of this study was to examine the differences in asymmetry indexes (AIs) of hippocampus between MDD patients and healthy controls (HCs) and their relationship with cognitive functions. Forty-one patients with first-episode drug-naïve MDD and 41 age- sex-matched HCs were recruited. All participants examined with 1.5T high-resolution magnetic resonance imaging. Two different methods for image analyses included manual method and FreeSurfer. Manual method was applied to analyze the longitudinal axis of hippocampal volumes, whereas FreeSurfer was used to analyze the hippocampal subfields. AIs were derived from the ratio of [left-right] to [left+right]. Cognitive functions which are composed of attention, memory, color trail test (CTT) and Wisconsin Card Sorting Test (WCST) were assessed. There were significant differences in AIs between two groups which were cornu amonis 1 (CA1) and CA4/dentate gyrus (DG). Differences in cognitive functions between groups included two sub-items in divided attention, six sub-items in word memory, one sub-item in facial memory, four sub-items in CTT and three sub-items in WCST. Partial correlation corrected by age, educational years and total intra-cerebral volume showed that there were significant correlations between CA1 and Faces1 True Positive of memory (r=-0.256, p=0.020) and Trails1 Time of CTT (r=-0.226, p=0.041), CA4/DG and Faces1 True Positive of memory (r=-0.301, p=0.006) and Trails1 Time of CTT (r=-0.247, p=0.025). Our results suggest AIs of CA1 and CA4/DG may play a crucial role in the cognitive dysfunction in MDD.

**Keywords:** hippocampus, asymmetry indexes, cognitive functions, major depressive disorders

**PS167**

Hemispheric differences in the relationship of serotonin transporter availability and hippocampal volumes in the human brain

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**Abstract**

Hippocampus and serotonin transporter (SERT) comes from two totally distinct systems but share a similar function, regulation of mood. Reduction of hippocampal volumes has been consistently reported in patient with major depressive disorder (MDD). Meanwhile, alteration of SERT, which terminates the serotonin action, has been implicated in the pathophysiology of MDD. However, the study of the functional and structural relationship between hippocampus and SERT was still limited. The aim of this study was to examine their relationship in the human brain. Six-four healthy subjects were recruited. All participants examined with 1.5T high-resolution magnetic resonance imaging. Image was analyzed by two different methods: manual and FreeSurfer. Manual method was applied to analyze the longitudinal axis of hippocampal volumes, which included head, body and tail body. FreeSurfer was used to analyze the volumes of hippocampal subfields. [123I-ADAM with single-photon emission computed tomography was applied for SERT imaging. Regions of interest included the midbrain, thalamus, caudate and putamen. Linear regression analysis was applied for the association of SERT and hippocampus. When took into account of age, sex and educational levels, SERT in the midbrain was associated with left total hippocampal volume (R²=0.15, adjusted R²=0.10, F=2.68, p=0.04), mainly contributed by body (β=0.33, t=2.66, p=0.01) and tail (β=0.31, t=2.55, p=0.013), but not right total hippocampal volume. In contrast, SERT in the thalamus was significantly associated with right total hippocampal volume (R²=0.15, adjusted R²=0.09, F=2.57, p=0.04), mainly contributed by head (β=0.32, t=2.5, p=0.02) but not left total hippocampus. There was no significant association between SERT and subfields of hippocampus. In conclusion, our results suggest that the association of serotonergic system and hippocampus is hemispheric different. A further study to test this idea in MDD is warrant.

**Key words:** hippocampus, serotonin transporter, SPECT

**PS168**

Hybrid PET/MR imaging of serotonin transporter occupancy and brain activation to elucidate the mechanism of action of selective serotonin reuptake inhibitors

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**Abstract**

While selective serotonin reuptake inhibitors (SSRIs) constitute first line therapy of depression and anxiety disorders, their mechanism of action remains to be elucidated. Hybrid PET/MR systems allow us to simultaneously probe the engagement of molecular targets and concomitant changes in brain activity following the application of psychopharmaceuticals. This study was aimed to establish imaging methods to be applied on clinical samples in the future.

**Methods:** 7 subjects underwent two measurements at the Biograph mMR scanner. [11C]DASB was applied as bolus plus constant infusion. After 60 minutes, double-blind infusion of 7.5mg cilupramoline or saline was performed and scanning was continued for 60 minutes, such that equilibrium was attained. An event-related emotion identification paradigm was performed before and after drug challenge. Serotonin transporter occupancy was calculated from binding potentials obtained using metabolite-corrected plasma activity at equilibrium and non-specific binding from cerebellum.

**Results:** Average serotonin transporter occupancy was 62% in the regions investigated (thalamus: 63±16%, amygdala: 61%±17%, midbrain: 54%±17%, putamen: 64±13%, nucleus caudatus: