あることが示唆された。

[参考文献]

1. 兼田康宏、住吉太幹、中込和幸、沼田周助、田中恒彦、上岡義典、大森哲郎、 Richard SE Keefe：統合失調症認知機能簡易評価尺度日本語版（BACS-J）、精神医学、50（９）、913-917、2008.
2. Y Kaneda, T Sumiyoshi, R Keefe, Y Ishimoto, S Numata, T Ohmori: The Brief Assessment of Cognition in Schizophrenia: validation of the Japanese version, Psychiatry and Clinical Neurosciences, 61（６）, P. 602-609, 2007.

F. 研究発表

１．論文発表

なし

２．学会発表など

なし

G. 知的財産権の出願・登録状況（予定も含む）

１．特許取得

なし

２．実用新案登録

なし

３．その他

なし

平成23年度　主任・分担研究者氏名一覧

「統合失調症における社会生活機能障害の評価・支援 -MATRICS-CCB 日本語版による認知機能障害の評価と治療計画への応用-」

区分	氏名	住所	所属	職名	e-mail
主任	曽良一郎	〒980-8574 宮城県仙台市青葉区星陵町1-1	東北大学大学院医学系研究科・精神・神経生物学分野	教授	sora@med.tohoku.ac.jp
分担	大森哲郎	〒770-8503 徳島市蔵本町 3-18-15	徳島大学大学院ヘルスバイオサイエンス研究部精神医学分野・精神医学	教授	tohmori@clin.med.tokushima-u.ac.jp
分担	住吉太幹	〒930-0194 富山県富山市杉谷2630	富山大学大学院医学薬学研究部・神経精神医学講座	准教授	sumiyo@med.u-toyama.ac.jp
分担	中込和幸	〒187-8551 小平市小川東町4-1-1	独立行政法人 国立精神・神経医療研究センター	上級専門職	nakagome@ncnp.go.jp
分担	松岡洋夫	〒980-8574 宮城県仙台市青葉区星陵町1-1	東北大学大学院医学系研究科精神神経学分野	教授	mtok-thk@umin.ac.jp
協力	住吉チカ	〒960-1296 福島県福島市金谷川1	福島大学人間発達文化学類	准教授	sumiyoshi@educ.fukushima-u.ac.jp
協力	兼田康宏	〒774-0014 徳島県阿南市学原町上水田11-1	岩城クリニック心療内科	院長	kaneday-tsh@umin.ac.jp

研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
Sumiyoshi T., Higuchi Y., Ito T., Kawasaki Y	Electrophysiological imaging evaluation of schizophrenia and treatment response. In: Handbook of Schizophrenia Spectrum Disorders; Vol III,	Ritsner M. (Ed)		Springer	New York,	2011	135-148
Sumiyoshi T., Uehara T.	Serotonin-1A receptors and cognitive enhancement in schizophrenia; Role for brain energy metabolism. In: Neuropsychiatric Disorders.	Burne T.H.J. (Ed)		InTech	Rijeka	in press	
Nekovarova T., Stuchlik A., Rambousek L., Vales K., Sumiyoshi T.	Cognitive deficits in rodent models of schizophrenia; Evaluation of spatial cognition. In: Schizophrenia Research: Recent Advances.	Sumiyoshi T. (Ed)		Nova Science Publishers	New York	in press	
Nakagome K, Mogami T.	9 Treatment-resistant schizophrenia. In Clinical Manual for Treatment of Schizophrenia.	Lauriello J and Pallanti S (eds.)		American Psychiatric Publishing	Washington DC	2012	341-380
Roberts DL, Penn DL, Combs DR.	「社会認知ならびに対人関係のトレーニング(SCIT Social Cognition and Interaction Training)」治療マニュアル	中込和幸, 兼子幸一, 最上多美子監訳		星和書店	東京	2011	
Kaneda Y, Ueoka Y, Sumiyoshi T, Yasui-Furukori N, Ito T, Higuchi Y, Kawamura I, Suzuki M, Ohmori T	The Schizophrenia Cognition Rating Scale Japanese version (SCoRS-J). In Yearbook of International Psychiatry and Behavioral Neurosciences-II.	Boutros N (Ed)		Nova Science Publishers	New York	in press	
曽良一郎	ドーパミン受容体 Dopamine receptor	ストレス科学辞典. 日本ストレス学会/(財)パブリックヘルスリサーチセンター監修		実務教育出版	東京	2011	764
曽良一郎	LSD-25	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	116

曽良一郎	逆耐性現象	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	215
曽良一郎	受容体	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	470
曽良一郎	ドーパミン	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	772
曽良一郎	ドーパミン仮説	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	773
曽良一郎	モノアミン仮説	加藤敏, 神庭重信, 中谷陽二, 武田雅俊, 鹿島晴雄, 狩野力八郎, 市川宏伸編	現代精神医学事典	弘文堂	東京	2011	1021-1022
曽良一郎, 氏家寛	物質依存の神経化学	福居顯二編集	脳とこころのプライマリケア第8巻 依存	シナジー	東京	2011	50-59
住吉太幹	非定形抗精神病薬の認知機能に対する効果.「統合失調症治療の新たなストラテジー」	石郷岡　純、岡崎　祐士、樋口輝彦　編		先端医学社	東京	2011	165-172
住吉太幹	統合失調症の認知機能はどこまで改善しうるか？「精神疾患と認知機能—最近の進歩」	山内俊雄　他編		新興医学出版社	東京	2011	31-41
住吉太幹	統合失調症の早期介入・発症予防における薬物療法.「向精神薬—最新の動向」.	野村総一郎　他編		医歯薬出版社	東京	2012	57-62

住吉太幹、樋口悠子	新規抗精神病薬の薬理、臨床応用：ペロスピロン.「《精神科臨床エキスパートシリーズ》『抗精神病薬完全マスター』」	中村 純 編		医学書院	東京	印刷中	
松岡洋夫	治療計画の策定(統合失調症：専門医をめざす人の精神医学.改訂第三版	山内俊雄,小島卓也、倉知正佳、鹿島晴雄編		医学書院	東京	2011	424-425
松岡洋夫	統合失調症の発症過程と認知機能：精神疾患と認知機能；最近の進歩	精神疾患と認知機能研究会編；編集総括 山内俊雄		新興医学出版	東京	2011	3-10
松岡洋夫、松本和紀	統合失調症の幻覚妄想	堀口淳編	脳とこころのプライマリ・ケア第6巻 幻覚と妄想	シナジー	東京	2011	30-38
兼田 康宏	統合失調症の認知機能検査(BACSなど)：精神疾患診断のための脳形態・機能検査	三国 雅彦 福田 正人 功刀 浩 編集		新興医学	東京	2012	77-83

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sumiyoshi T., Higuchi Y., Matsui M., Itoh H, Itoh T., Arai H, Chieko Takamiya C. Uehara T., Suzuki M., Kurachi M.	Membrane fatty acid levels as a predictor of treatment response in schizophrenia.	Psychiatry Research	186	23-27	2011
Itoh T., Sumiyoshi T., Higuchi Y., Suzuki M., Kawasaki Y.	LORETA analysis of three-dimensional distribution of delta-band activity in schizophrenia: Relation to negative symptoms.	Neuroscience Research	70	442-8	2011
Uehara T., Sumiyoshi T., Hattori H., Itoh H., Matsuoka T., Iwakami N, Suzuki M., Kurachi M.	T-817MA, a novel neurotrophic agent, ameliorates loss of GABAergic parvalbumin-positive neurons and sensorimotor gating deficits in rats transiently exposed to MK-801 in the neonatal period.	Journal of Psychiatric Research			in press

Uehara T., Itoh H., Matsuoka T., Rujescu D., Genius J., Seo T., Sumiyoshi T.	Neonatal MK-801 treatment suppresses stress-induced lactate metabolism in the medial prefrontal cortex of adult rats: Role of 5-HT1A receptors.	Synapse			in press
Pu S, Yamada T, Yokoyama K, Matsumura H, Kobayashi H, Sasaki N, Mitani H, Adachi A, Kaneko K, Nakagome K.	A multi-channel near-infrared spectroscopy study of prefrontal cortex activation during working memory task in major depressive disorder.	Neurosci Res.	70(1)	91-97	2011
Ikezawa S, Mogami T, Hayami Y, Sato I, Kato T, Kimura I, Pu S, Kaneko K, Nakagome K.	The pilot study of a Neuropsychological Educational Approach to Cognitive Remediation for patients with schizophrenia in Japan.	Psychiatry Res.	195(3)	107-110	2011
Sumiyoshi C., Ertugrul A., Anil Yagcioglu A.E., Sumiyoshi T.	Semantic memory deficits based on category fluency performance in schizophrenia: Similar impairments across Turkish and Japanese patients	Psychiatry Research	167	47-57	2009
Sumiyoshi, C., Kawakubo, Y., Suga, M., Sumiyoshi, T. & Kasai, K.:	Impaired ability to organize information in individuals with autism spectrum disorders and their siblings	Neuroscience Research	69	252-257	2011
Tenjin T, Miyamoto S, Miyake N, Ogino S, Kitajima R, Ojima K, Arai J, Teramoto H, Tsukahara S, Ito Y, Tadokoro M, Anai K, Funamoto Y, Kaneda Y, Sumiyoshi T, Yamaguchi N.	Effect of blonanserin on cognitive function in antipsychotic-naïve first-episode schizophrenia.	Human Psychopharmacology	27	90-100	2012
Yoshida T, Suga M, Arima K, Muranaka Y, Tanaka T, Eguchi T, Lin C, Yoshida S, Ishikawa M, Higuchi Y, Seo T, Ueoka Y, Tomotake M, Kaneda Y, Darby D, Maruff P, Iyo M, Kasa K, Higuchi T, Sumiyoshi T, Ohmori T, Takahashi K, Hashimoto K.	Criterion and Construct Validity of the CogState Schizophrenia Battery in Japanese Patients with Schizophrenia.	PLoS One.	6(5)	e20469	2011
Tenjin T, Miyamoto S, Miyake N, Ogino S, Kitajima R, Ojima K, Arai J, Teramoto H, Tsukahara S, Fujiwara K, Funamoto Y, Ito Y, Tadokoro M, Anai K, Kaneda Y, SumiyoshiT, Yamaguchi N.:	Effect of blonanserin on cognitive function in antipsychotic-naïve first-episode schizophrenia.	Human Psychopharmacology: Clinical and Experimental.			in press

曽良一郎	ドロキシドパのAD/HDへの効果	週刊日本医事新報	4534	99-100	2011
曽良一郎	精神科治療薬の被災地への提供	艮陵新聞	(平成22年度第3・4号) 第272・273合併号	7	2011
曽良一郎	総括研究報告　統合失調症における社会生活機能障害の評価・支援　-MATRICS-CCB 日本語版による認知機能障害の評価と治療計画への応用-. 厚生労働科学研究費補助金（障害者対策総合研究事業（精神障害分野））統合失調症における社会生活機能障害の評価・支援-MATRICS-CCB 日本語版による認知機能障害の評価と治療計画への応用	平成22年度総括・分担研究報告書		1-4	2011
曽良一郎，内海修，有銘預世布，福井麻美，笠原好之	注意欠如多動性障害（AD/HD）、統合失調症動物モデルを用いた認知機能障害へのニコチン性神経伝達による治療メカニズムの解明	平成22年度喫煙科学研究財団研究年報		559-564	2011
曽良一郎，宮澤志保，東海林渉，佐藤拓，佐藤修哉，佐藤愛，鈴木大輔，田邊陽一郎，住吉チカ，住吉太幹，兼田康宏，上埜高志，大森哲郎，中込和幸	分担研究報告　MCCB　日本語版による社会生活機能の評価. 厚生労働科学研究費補助金（障害者対策総合研究事業（精神障害分野））統合失調症における社会生活機能障害の評価・支援 -MATRICS-CCB 日本語版による認知機能障害の評価と治療計画への応用	平成22年度 総括分担研究報告書		5-15	2011
山田清文，曽良一郎，池田和隆	JSNP東日本大震災対策WG　宮城県仙台市-石巻　視察報告書	日本神経精神薬理学雑誌	31 (3)	141-145	2011
笠原好之，有銘預世布，福井麻美，久保有美子，曽良一郎	統合失調症動物モデルにおける神経回路の形成・発達の解析	精神薬療研究年報	43	73-74	2011

総説

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Kobayashi H, Ujike H, Iwata N, Inada T, Yamada M, Sekine Y, Uchimura N, Iyo M, Ozaki N, Itokawa M, Sora I.	Association analysis of the Adenosine A1 receptor gene polymorphisms in patients with methamphetamine dependence/psychosis.	Current Neuropharmacology	9	137-142	2011
Kobayashi H, Ujike H, Iwata N, Inada T, Yamada M, Sekine Y, Uchimura N, Iyo M, Ozaki N, Itokawa M, Sora I.	Association analysis of the Tryptophan Hydroxylase 2 gene polymorphisms in patients with methamphetamine dependence/psychosis.	Current Neuropharmacology	9	176-182	2011

Ide S, Minami M, Uhl GR, Satoh M,Sora I,Ikeda K.	(-)-Pentazocine induces visceral chemical antinociception, but not thermal, mechanical, or somatic chemical antinociception, in mu-opioid receptor knockout mice.	Molecular Pain	7(1)	23	2011
Yoshimura T, Usui H, Takahashi N, Yoshimi A, Saito S, Aleksic B, Ujike H, Inada T, Yamada M, Uchimura N, Iwata N, Sora I, Iyo M, Ozaki N.	Association analysis of the GDNF gene with methamphetamine use disorder in a Japanese population.	Prog Neuropsychopharmacol Biol Psychiatry	35(5)	1268-72	2011
Yamamoto H, Takamatsu Y, Imai K, Kamegaya E, Hagino Y, Watanabe M, Yamamoto T, Sora I, Koga H, Ikeda K.	Mop reduction during long-term methamphetamine withdrawal was restored by chronic post-treatment with fluoxetine.	Current Neuropharmacology	9	73-78	2011
Hagino Y, Takamatsu Y, Yamamoto H, Iwamura T, Murphy DL, Uhl GR, Sora I, Ikeda K.	Effect of MDMA on extracellular dopamine and serotonin levels in mice lacking dopamine and/or serotonin transporters.	Current Neuropharmacology	9	91-95	2011
Kasai S, Yamamoto H, Kamegaya E, Uhl GR, Sora I, Watanabe M, Ikeda K.	Quantitative detection of m opioid receptor: Western blot analyses using m opioid receptor knockout mice.	Current Neuropharmacology	9	219-222	2011
Komatsu H, Ohara A, Sasaki K, Abe H, Hattori H, Hall FS, Uhl GR, Sora I.	Decreased response to social defeat stress in μ-opioid-receptor knockout mice.	Pharmacology Biochemistry & Behavior	99	676-682	2011
Sogawa C, Sogawa N, Ohyama K, Kikura-Hanajiri R, Goda Y, Sora I, Kitayama S.	Methylone and monoamine transporters: correlation with toxicity.	Current Neuropharmacology	9	58-62	2011
Okahisa Y, Kodama M, Takaki M, Inada T, Uchimura N, Yamada M, Iwata N, Iyo M, Sora I, Ozaki N, Ujike H.	Association between the Regulator of G-protein Signaling 9 Gene and Patients with Methamphetamine Use Disorder and Schizophrenia.	Curr Neuropharmacol	9(1)	190-194	2011
Okahisa Y, Kodama M, Takaki M, Inada T, Uchimura N, Yamada M, Iwata N, Iyo M, Sora I, Ozaki N, Ujike H.	Association Study of Two Cannabinoid Receptor Genes, CNR1 and CNR2, with Methamphetamine Dependence.	Curr Neuropharmacol	9(1)	183-189	2011

Yokobayashi E, Ujike H, Kotaka T, Okahisa Y, Takaki M, Kodama M, Inada T, Uchimura N, Yamada M, Iwata N, Iyo M, Sora I, Ozaki N, Kuroda S.	Association study of serine racemase gene with methamphetamine psychosis.	Curr Neuropharmacol	9(1)	169-175	2011
Ujike H, Kishimoto M, Okahisa Y, Kodama M, Takaki M, Inada T, Uchimura N, Yamada M, Iwata N, Iyo M, Sora I, Ozaki N.	Association Between 5HT1b Receptor Gene and Methamphetamine Dependence.	Curr Neuropharmacol	9(1)	163-168	2011
Tsunoka T, Kishi T, Ikeda M, Kitajima T, Yamanouchi Y, Kinoshita Y, Kawashima K, Okochi T, Okumura T, Inada T, Ujike H, Yamada M, Uchimura N, Sora I, Iyo M, Ozaki N, Iwata N.	No Association Between GRM3 and Japanese Methamphetamine-Induced Psychosis.	Curr Neuropharmacol	9(1)	160-162	2011
Okumura T, Okochi T, Kishi T, Ikeda M, Kitajima T, Kinoshita Y, Kawashima K, Tsunoka T, Fukuo Y, Inada T, Yamada M, Uchimura N, Iyo M, Sora I, Ozaki N, Ujike H, Iwata N.	Genetic Association Analysis of NOS1 and Methamphetamine-Induced Psychosis Among Japanese.	Curr Neuropharmacol	9(1)	155-159	2011
Okochi T, Kishi T, Ikeda M, Kitajima T, Kinoshita Y, Kawashima K, Okumura T, Tsunoka T, Fukuo Y, Inada T, Yamada M, Uchimura N, Iyo M, Sora I, Ozaki N, Ujike H, Iwata N.	Genetic Association Analysis of NOS3 and Methamphetamine-Induced Psychosis Among Japanese.	Curr Neuropharmacol	9(1)	151-154	2011
Kishi T, Kitajima T, Tsunoka T, Okumura T, Kawashima K, Okochi T, Yamanouchi Y, Kinoshita Y, Ujike H, Inada T, Yamada M, Uchimura N, Sora I, Iyo M, Ozaki N,	Lack of association between prokineticin 2 gene and Japanese methamphetamine dependence.	Curr Neuropharmacol	9(1)	133-136	2011
Kishi T, Kitajima T, Kawashima K, Okochi T, Yamanouchi Y, Kinoshita Y, Ujike H, Inada T, Yamada M, Uchimura N, Sora I, Iyo M, Ozaki N, Iwata N.	Association Analysis of Nuclear Receptor Rev-erb Alpha Gene (NR1D1) and Japanese Methamphetamine Dependence.	Curr Neuropharmacol	9(1)	129-132	2011
Kishi T, Fukuo Y, Okochi T, Kitajima T, Ujike H, Inada T, Yamada M, Uchimura N, Sora I, Iyo M, Ozaki N, Correll CU, Iwata N.	No significant association between SIRT1 gene and methamphetamine-induced psychosis in the Japanese population.	Hum Psychopharmacol.	26(7)	445-450	2011
Arime Y, Kubo Y, Sora I.	Animal models of attention-deficit/hyperactivity disorder .	Biol. Pharm. Bull.	34(9)	1373-1376	2011

Okuyama K, Ide S, Sakurada S, Sasaki K, Sora I, Tamura G, Ohkawara Y, Takayanagi M, Ohno I.	μ-opioid Receptor-Mediated Alterations of Allergen-Induced Immune Responses of Bronchial Lymph Node Cells in a Murine Model of Stress Asthma.	Allergol Int			2011
Kishi T, Ikeda M, Kitajima T, Yamanouchi Y, Kinoshita Y, Kawashima K, Inada T, Harano M , Komiyama T, Hori T, Yamada M, Iyo M, Sora I, Sekine Y, Ozaki N, Ujike	No association between prostate apoptosis response 4 gene (PAWR) and methamphetamine use disorder in the Japanese population	Ann. N.Y. Acad. Sci？			in press
Hall FS, Axelrad S, Hoggatt IH, Roff S, Sora I, Hen R, Uhl GR.	Complementation of serotonin receptor 1B knockout and dopamine transporter gene knockouts on cocaine locomotion.	Submitted to Neuropsychopharmacology			
Itokawa K, Moessner R, Sora I, Lesch KP, Hall FS, Uhl GR.	Dopaminergic aging is accelerated in mice with heterozygous knockout of vesicular monoamine transporter (VMAT2) but not dopamine transporter (DAT).	Submitted to Neuroscience			
Ohara A, Hata H, Kobayashi H, Numachi Y, Yamamoto H, Miyoshi I, Hall FS, Uhl GR, Tomita H, Sora I.	Exclusive expression of VMAT2 in noradrenergic neurons increases viability of homozygous VMAT2 knockout mice.	Submitted to Psychopharmacology			
Yamamoto H, Takamatsu Y, Imai K, Kamegaya E, Hagino Y, Watanabe M, Yamamoto T, Sora I, Koga H, Ikeda K.	Reduced conditioned place preference for methamphetamine and methamphetamine-induced changes in μ opioid receptor gene expression inthe mouse frontal cortex by fluoxetine treatment.	Submitted to Journal of Neurochemistry			
Yu Z, Ono C, Kim HB, Komatsu H, Tanabe Y, Sakae N, Nakayama KI, Matsuoka H, Sora I, Bunney WE, Tomita H.	Four mood stabilizers commonly induce FEZ1 expression in human astrocytes.	Bipolar Disord	13(5-6)	486-99	2011
Tomotake M.	Quality of life and its predictors in people with schizophrenia.	J med Invest.	58(3-4)	167-174	2011
曽良一郎	カテコールアミン神経伝達．認知症学（上）その解明と治療の最新知見	日本臨床	69増刊号8	224-227	2011

曽良一郎	シンポジウム特集「認知機能障害に対する治療をどう評価するか」	日本神経精神薬理学雑誌	31	239	2011
佐藤拓, 曽良一郎	MATRICSコンセンサス認知機能評価バッテリー日本語版の開発への取り組み	日本神経精神薬理学雑誌	31	241-244	2011
住吉 太幹　兼田 康宏　住吉 チカ　曽良 一郎	認知機能評価システムの構築-MATRICS-CCB-J, BACS-Jおよび社会機能測定法について	精神科治療学	26(12)	1525-1531	2011
住吉太幹	統合失調症の早期介入・発症予防における薬物療法.	医学のあゆみ	236(10)	949-955	2011
最上多美子, 池澤聰, 兼子幸一, 朴盛弘, 中込和幸.	統合失調症の認知機能障害に対する認知矯正療法の効果	日本神経精神薬理学雑誌	31	245-249	2011
松岡洋夫	若者のメンタルヘルスケアに向けて:精神病の早期介入研究から見えてきたこと.	精神神経学雑誌			印刷中
松岡洋夫	統合失調症顕在発症前のリスク状態.	児童青年精神医学とその近接領域			印刷中
松岡洋夫	統合失調症における機能障害の病態と治療.	精神医学	53(2)	111-117	2011
住吉チカ	統合失調症患者における機能的転帰:MATRICS Consensus Cognitive Batteryとの関連.	日本神経精神薬理学雑誌	31	249–256	2011
住吉チカ	子どもの学習から考えるこころと脳—読みの習得とその障害	こころの科学	150	43- 48	2010
兼田康宏、上岡義典、住吉太幹、古郡規雄、伊東徹、樋口悠子、鈴木道雄、大森哲郎	統合失調症認知評価尺度日本語版を用いたco-primaryの測定.	日本神経精神薬理学雑誌	31	259-62	2011

研究成果の刊行物・別刷

Association Analysis of the Adenosine A1 Receptor Gene Polymorphisms in Patients with Methamphetamine Dependence/Psychosis

Hideaki Kobayashi[1,$], Hiroshi Ujike[2,11], Nakao Iwata[3,11], Toshiya Inada[4,11], Mitsuhiko Yamada[5,11], Yoshimoto Sekine[6,11], Naohisa Uchimura[7,11], Masaomi Iyo[8,11], Norio Ozaki[9,11], Masanari Itokawa[10] and Ichiro Sora[1,11,*]

[1]Department of Biological Psychiatry, Tohoku University Graduate School of Medicine, Sendai 980-8574, Japan; [2]Department of Neuropsychiatry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan; [3]Department of Psychiatry, Fujita Health University School of Medicine, Aichi 470-1192, Japan; [4]Department of Psychiatry, Seiwa Hospital, Institute of Neuropsychiatry, Tokyo 162-0851, Japan; [5]Department of Psychogeriatrics, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo 187-8553, Japan; [6]Division of Medical Treatment & Rehabilitation, Center for Forensic Mental Health, Chiba University, Chiba 260-8670, Japan; [7]Department of Neuropsychiatry, Kurume University School of Medicine, Kurume 830-0011, Japan; [8]Department of Psychiatry, Graduate School of Medicine, Chiba University, Chiba 260-8670, Japan; [9]Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya 466-8550, Japan; [10]Schizophrenia Research Project, Tokyo Institute of Psychiatry, Tokyo 156-8585, Japan; [11]Japanese Genetics Initiative for Drug Abuse (JGIDA), Japan;

Abstract: Several lines of evidence suggest that the dopaminergic nervous system contributes to methamphetamine (METH) dependence, and there is increasing evidence of antagonistic interactions between dopamine and adenosine receptors in METH abusers. We therefore hypothesized that variations in the A1 adenosine receptor (*ADORA1*) gene modify genetic susceptibility to METH dependence/psychosis. In this study, we identified 7 single nucleotide polymorphisms (SNPs) in exons and exon-intron boundaries of the *ADORA1* gene in a Japanese population. A total of 171 patients and 229 controls were used for an association analysis between these SNPs and METH dependence/psychosis. No significant differences were observed in either the genotypic or allelic frequencies between METH dependent/psychotic patients and controls. A global test of differentiation among samples based on haplotype frequencies showed no significant association. In the clinical feature analyses, no significant associations were observed among latency of psychosis, prognosis of psychosis, and spontaneous relapse. These results suggest that the *ADORA1* gene variants may make little or no contribution to vulnerability to METH dependence/psychosis.

Keywords: Single nucleotide polymorphism, SNP, variation, human, Japanese, MAP, abuse, dopamine.

INTRODUCTION

Methamphetamine (METH) is a psychomotor stimulant with high liability for abuse, and METH abuse has become a very serious social problem in Japan [1]. Chronic METH abusers have been shown to have persistent dopaminergic deficits [2, 3]. Amphetamines are thought to produce their stimulant effects mainly *via* the dopaminergic system [4, 5], although other systems may also be involved. Dopamine D1 and D2 receptors form heterodimeric complexes with adenosine A1 and A2a receptors respectly, which modulate their responsiveness [6-9], suggesting that responses to amphetamines may also depend on adenosinergic function.

Several lines of evidence suggest that adenosine A1 receptors play a role in inhibiting the effects of METH. Adenosine receptor antagonists potentiate the effects of lower METH doses and substitute for the discriminative stimulus effects of METH [10, 11]. Adenosine receptor agonists protect against METH-induced neurotoxicity, and amphetamine-induced stereotypy and locomotor activity, and reduce the acquisition of conditioned place preference induced by amphetamine [12-15]. These results suggest that adenosine A1 receptors play important roles in the expression of METH-induced neurotoxicities and behaviors.

To date, however, there has been no association analysis between A1 adenosine receptor (*ADORA1*) gene variants and drug addiction. The purpose of this study was (1) to identify novel sequence variants in all coding exons as well as exon-intron boundaries of the *ADORA1* gene in Japanese, and (2) to investigate whether these polymorphisms and/or haplotypes were associated with METH dependence/psychosis.

MATERIALS AND METHODS

Subjects

One-hundred seventy-one unrelated patients with METH dependence/psychosis (138 males and 33 females; mean age 37.5±12.0 years) meeting ICD-10-DCR criteria (F15.2 and F15.5) were used as case subjects; they were outpatients or inpatients of psychiatric hospitals. The 229 control subjects (119 males and 110 females; mean age 41.2±12.3 years) were mostly medical staff members who had neither per-

*Address correspondnce to this author at the Department of Biological Psychiatry, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai, 980-8574, Japan; Tel: +81-22-717-7808; Fax: +81-22-717-7809; E-mail: sora@med.tohoku.ac.jp

[$]Current address: Research Unit of Genome New Drugs, School of Pharmacy, Nihon University, Chiba 274-8555, Japan

1570-159X/11 $58.00+.00

sonal nor familial history of drug dependence or psychotic disorders, as verified by a clinical interview. All subjects were Japanese, born and living in the northern Kyushu, Setouchi, Chukyo, Tokai, and Kanto regions. This study was approved by the ethical committees of each institute of the Japanese Genetics Initiative for Drug Abuse (JGIDA), and all subjects provided written informed consent for the use of their DNA samples for this research [16]. After informed consent was obtained, blood samples were drawn and genomic DNA was extracted by the phenol/chloroform method.

Defining Variants of the *ADORA1* Gene

Initially, DNA samples from 16 METH dependent/psychotic patients were used to identify nucleotide variants within the *ADORA1* gene (GenBank accession no. AC105940). Exon numbers were based on the report by Ren and colleagues [17]. Exons 1A, 1B, 2, 3 and exon-intron boundaries were amplified by polymerase chain reaction (PCR) using a thermal cycler (Astec, Fukuoka, Japan), and the products were sequenced in both directions using BigDye terminators (Applied Biosystems, Foster City, CA) by an ABI Genetic analyzer 3100 (Applied Biosystems). The primer sequences used in this study are shown in Table **1**.

Genotyping of IVS1A+182 (rs56298433) was performed by PCR amplification using 2F-2R primers followed by restriction enzyme *Nla* III digestion. Genotyping of Exon2+363 (rs10920568) was performed by PCR amplification using 4F-4R primers followed by sequencing with the same primers. IVS2+35826 (rs5780149) was performed by PCR amplification using 5F-9R primers followed by sequencing with 5F and 5R primers. Genotyping of Exon3+937 (rs6427994), Exon3+987 (rs41264025), and Exon3+1064 (rs16851030) was performed by PCR amplification using 5F-9R primers followed by sequencing with 7F and 7R primers.

Patient Subgroups

For the clinical category analysis, the patients were divided into two subgroups by three different clinical features. (A) Latency of psychosis from first METH intake: less than 3 years or more than 3 years. The course of METH psychosis varied among patients, with some patients showing psychosis sooner after the first METH intake, as previously reported [16, 18]. Because the median latency was 3 years, this time point was used as the cutoff in defining the two groups. (B) Duration of psychosis after the last METH intake: transient (<1 month) or prolonged (≧1 month). Some patients showed continuous psychotic symptoms even after METH discontinuation, as previously reported [16, 18]. Patients with the transient type showed a reduction of psychotic symptoms within one month after the discontinuation of METH consumption and the beginning of treatment with neuroleptics. Patients with the prolonged type showed a psychotic symptoms continued for more than one month even after the discontinuation of METH consumption and the beginning of neuroleptic treatment. (C) Spontaneous relapse: present or not. It has been well documented that once METH psychosis has developed, patients in the remission phase are liable to spontaneous relapse without reconsumption of METH [16, 18].

Statistical Analysis

The Hardy-Weinberg equilibrium of genotypic frequencies in each SNP was tested by the chi-square test. The level of statistical significance was set at $\alpha = 0.05$. The allelic and genotypic frequencies of the patient and control groups were compared using the chi-square test. Haplotype frequencies were calculated by the Arlequin program available from http://anthropologie.unige.ch/arlequin [19]. Locus by locus linkage disequilibrium (LD) was evaluated by D' and r^2, which were calculated by the haplotype frequencies using the appropriate formula in the Excel program. A global test of differentiation among samples based on haplotype frequencies was also performed by the Arlequin program.

RESULTS

Analysis of the *ADORA1* Gene Variants

To identify polymorphisms in the *ADORA1* gene, exons 1A, 1B, 2, and 3, and exon-intron boundaries were analyzed using genomic DNA from Japanese METH dependent/psychotic subjects. Seven SNPs were identified (Table **2**). Five out of seven of these SNPs were previously reported by Deckert [20]. In the two SNPs, the frequencies of the minor

Table 1. Primers Used in this Study

Exon	Forward		Reverse	
Exon1A	1F:	TGG ACT GGA TGC CTT ATG GCT TAG	1R:	GGC GCA GGA GCT GAG TGA CAA TCG
	2F:	TCT CAC CCA GTA TCA CTT CCT TTG	2R:	ATC ACA TGG TAC GGC AGA GAC TCA
Exon1B	3F:	AAT AGG GAG AAA CGC CCC AGC CTT	3R:	AAG CAC CTG TGT GGT CAG GGA AGC
Exon2	4F:	GGT AGG AGC TGC ATG TGA CAA GTG	4R:	GCA GAG TGA GGA CTG GAG CAC GAT
Exon3	5F:	GGC TGT CAT GAA GCA ATG ATG AGA	5R:	CCA GCG ACT TGG CGA TCT TCA GCT
	6F:	TCT ACC TGG AGG TCT TCT ACC TAA	6R:	CCC TGA AGC TCT GGA CTG CTC ATG
	7F:	GTG GTC CCT CCA CTA GGA GTT AAC	7R:	ACA GGT AAT TAC ACT CCA AGG CTC
	8F:	CTG ATA TTT GCT GGA GTG CTG GCT	8R:	ACA CCT GCA ACA GAG CTT CCA AAG
	9F:	CCT TGC TGT CAT GTG AAT CCC TCA	9R:	CAA GAG GAA GAT GCC AAT GGG AGA

alleles differed between our patients and those of Deckert. In the Exon2+363 (rs10920568) SNP, the G allele was present in 15.5% of our Japanese controls (Table **3**) and 36.9% of the German controls [20]. In the Exon3+1064 (rs16851030) SNP, the T allele was present in 35.8% of our Japanese controls and 1.2% of the German controls [20]. These differences were suggested to be related to the difference in ethnicity between the two cohorts. One SNP, Exon2+363 (rs10920568), was a synonymous mutation (Ala to Ala) (Table **2**). All the other SNPs were located either in the introns or an untranslated region in the exon 3. Two SNPs (Exon3+937 (rs6427994) and Exon3+1454 (rs11315020)) were in linkage disequilibrium (LD) in the sense that the genotypic patterns of the 16 samples examined were the same, representing Exon3+937 (rs6427994) for these two SNPs. IVS1A+182 (rs56298433), Exon2+363 (rs10920568), IVS2+35826 (rs5780149), Exon3+937 (rs6427994), Exon3+987 (rs41264025), and Exon3+1064 (rs16851030) were chosen for further analysis.

Table 2. ***ADORA1*** **Gene Variants Found in the Japanese Population**

Location	Variants	rs#	SNP Name	Function
IVS1A+182	G/T	rs56298433		intron
Exon2+363	T/G	rs10920568	805T/G	synonymous (Ala->Ala)
IVS2+35826	T4/T5	rs5780149		intron
Exon3+937	A/C	rs6427994	1777C/A	untranslated
Exon3+987	C/T	rs41264025	1827C/T	untranslated
Exon3+1064	C/T	rs16851030	1904C/T	untranslated
Exon3+1454	T/del	rs11315020	2294insT	untranslated

The nucleotide sequence of the *ADORA1* gene was refereneed to the NCBI nucleotide database under accession number AC105940. Exon numbers were based on the report by Ren and colleagues [17]. The column labelled rs# shows SNP numbers from the NCBI SNP database. The data in the column labelled SNP name are from the report by Deckert [20].

Table 3. Genotypic and Allelic Distribution of the *ADORA1* Gene SNPs in the METH Subjects and the Controls

SNP	Group	N	Genotype (%)			P	Allele (%)		P
IVS1A+182 (rs56298433)			G	G/T	T		G	T	
	Control	224	222 (99.1%)	2 (0.9%)	0 (0.0%)	0.961	446 (99.6%)	2 (0.4%)	0.823
	METH	168	166 (98.8%)	2 (1.2%)	0 (0.0%)		334 (99.4%)	2 (0.6%)	
Exon2+363 (rs10920568)			T	T/G	G		T	G	
	Control	229	162 (70.7%)	63 (27.5%)	4 (1.7%)	0.333	387 (84.5%)	71 (15.5%)	0.233
	METH	171	132 (77.2%)	36 (21.1%)	3 (1.8%)		300 (87.7%)	42 (12.3%)	
IVS2+35826 (rs5780149)			T4	T4/T5	T5		T4	T5	
	Control	229	150 (65.5%)	69 (30.1%)	10 (4.4%)	0.887	369 (80.6%)	89 (19.4%)	0.708
	METH	171	108 (63.2%)	55 (32.2%)	8 (4.7%)		271 (79.2%)	71 (20.8%)	
Exon3+937 (rs6427994)			A	A/C	C		A	C	
	Control	229	2 (0.9%)	46 (20.1%)	181 (79.0%)	0.248	50 (10.9%)	408 (89.1%)	0.222
	METH	171	5 (2.9%)	38 (22.2%)	128 (74.9%)		48 (14.0%)	294 (86.0%)	
Exon3+987 (rs41264025)			C	C/T	T		C	T	
	Control	229	215 (93.9%)	14 (6.1%)	0 (0.0%)	0.937	444 (96.9%)	14 (3.1%)	0.888
	METH	171	162 (94.7%)	9 (5.3%)	0 (0.0%)		333 (97.4%)	9 (2.6%)	
Exon3+1064 (rs16851030)			C	C/T	T		C	T	
	Control	229	89 (38.9%)	116 (50.7%)	24 (10.5%)	0.071	294 (64.2%)	164 (35.8%)	0.572
	METH	171	80 (46.8%)	67 (39.2%)	24 (14.0%)		227 (66.4%)	115 (33.6%)	

N: number of samples.
P: Significance values between the METH subjects and the controls.

Relationship Between the *ADORA1* Gene SNPs and METH Dependence/Psychosis

Association analyses between these SNPs in the *ADORA1* gene and METH dependence/psychosis were performed using DNA samples from 171 METH dependent/psychotic subjects and 214 control subjects (Table **3**). Among them, the genotypes of five control samples and three METH samples could not be determined at IVS1A+182 (rs56298433). The genotypic frequencies in these SNPs were within the Hardy-Weinberg expectations. No significant differences of the genotypic and allelic distributions of these SNPs in these samples were observed. As the minor allele frequencies of two SNPs, IVS1A+182 (rs56298433) and Exon3+987 (rs41264025), were less than 5%, another four SNPs, Exon 2+363 (rs10920568), IVS2+35826 (rs5780149), Exon3+937 (rs6427994), and Exon3+1064 (rs16851030), were used for further analyses.

A global test of differentiation among samples based on haplotype frequencies was performed using the Arlequin program, but no significant association with METH dependence/psychosis was observed (P=0.590). Haplotype frequencies were estimated by the Arlequin program, and locus by locus LD was calculated by using the appropriate formula in the Excel program. Most of the SNPs in exon 2 and exon 3 were in LD, suggesting that the locus from exon 2 to exon 3 was in a LD block (Table **4**).

Subcategory analyses were conducted on the clinical parameters (latency of psychosis, prognosis of psychosis, and spontaneous relapse) (Table **5**). Significant differences were observed in the shorter latency of psychosis (P=0.025) at Exon3+937 (rs6427994). However, this significance disappeared after Bonferroni correction by the sub-group numbers, two ($P < 0.025$).

DISCUSSION

We analyzed the *ADORA1* gene variations in a Japanese population and found seven SNPs in exons and exon-intron boundaries. However, no significant associations were

Table 4. Linkage Disequilibrium Mapping of the *ADORA1* Gene

	Exon2+363 (rs10920568)	**IVS2+35826 (rs5780149)**	**Exon3+937 (rs6427994)**	**Exon3+1064 (rs16851030)**	
Exon2+363		0.807	0.729	0.374	
IVS2+35826	0.029		1.000	0.676	D'
Exon3+937	0.012	0.030		1.000	
Exon3+1064	0.014	0.061	0.068		
			r^2		

D' and r^2 values for Controls are shown in the upper right and lower left, respectively.

Table 5. Genotypic Distribution of the *ADORA1* Gene SNPs in Subcategorized METH Subjects

		SNP	**Exon2+363 (rs10920568)**				**IVS2+35826 (rs5780149)**				**Exon3+937 (rs6427994)**				**Exon3+1064 (rs16851030)**			
		Genotype	**T**	**T/G**	**G**		**T4**	**T4/T5**	**T5**		**A**	**A/C**	**C**		**C**	**C/T**	**T**	
Group		**N**				**P**				**P**				**P**				**P**
Control		229	162	63	4		150	69	10		2	46	181		89	116	24	
METH	Latency of Psychosis																	
	<3 years	67	48	16	3	0.387	46	17	4	0.684	4	10	53	0.025	30	26	11	0.173
	≧3 years	71	56	15	0	0.275	40	29	2	0.229	0	22	49	0.124	35	28	8	0.237
	Prognosis of Psychosis																	
	Transient (<1 month)	91	70	19	2	0.465	59	29	3	0.883	3	22	66	0.190	42	37	12	0.269
	Prolonged (≧1 month)	56	41	14	1	0.932	33	20	3	0.654	1	11	44	0.835	27	21	8	0.205
	Spontaneous Relapse																	
	Not present	104	81	22	1	0.381	64	34	6	0.733	4	25	75	0.107	52	39	13	0.081
	Present	60	45	13	2	0.519	39	19	2	0.923	1	11	48	0.831	25	24	11	0.163

N: number of samples.
P: Significance values between the METH subjects and the controls.

observed between these SNPs and METH dependence/psychosis in the genotypic, allelic, haplotypic or clinically subcategorized analyses.

This is the first association analysis between *ADORA1* gene variants and drug addiction. We failed to find associations between the *ADORA1* gene SNPs and METH dependence/psychosis. While the significant difference (P=0.025) in the shorter latency of psychosis at Exon3+937 (rs6427994) disappeared after Bonferroni correction, this may have been due to the sample size, and thus further analysis with a larger sample is warranted.

The variants we found were one synonymous SNP, two intron SNPs and four exon SNPs in the untranslated region. These SNPs are unlikely to affect receptor function because they are not non-synonymous SNPs or promoter SNPs. Because several animal studies have suggested a modulatory role of adenosine receptors for dopamine systems, it remains possible that another region in the *ADORA1* gene, such as a promoter region or intron regions, contributes to the alteration of *ADORA1* gene function.

Although a few association analyses of the *ADORA1* gene and psychiatric diseases have been performed, no significant association has been reported between *ADORA1* variants and bipolar affective disorder or panic disorder [20, 21]. As caffeine is a nonselective adenosine receptor antagonist, the association between the psychoactive effects of caffeine and gene variants of adenosine receptors have also been studied. However, the anxiogenic response to an acute dose of caffeine in healthy, infrequent caffeine users was not associated with *ADORA1* gene polymorphism [22]. Interindividual variation in the anxiety response to amphetamine has also been studied in healthy volunteers, but no association was observed with *ADORA1* gene variants [23]. These results suggest that the *ADORA1* gene variations have little effect on psychiatric symptoms and/or personality traits.

In conclusion, our data suggest that the *ADORA1* gene variants may not play a major role in the development of METH dependence/psychosis.

ACKNOWLEDGEMENTS

We thank all the subjects who participated in this study. This study was supported in part by a Grant-in-Aid for Health and Labor Science Research (Research on Pharmaceutical and Medical Safety) from the Ministry of Health, Labor and Welfare of Japan; and by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

REFERENCES

[1] Matsumoto, T.; Kamijo, A.; Miyakawa, T.; Endo, K.; Yabana, T.; Kishimoto, H.; Okudaira, K.; Iseki, E.; Sakai, T.; Kosaka, K. Methamphetamine in Japan: the consequences of methamphetamine abuse as a function of route of administration. *Addiction,* **2002**, *97*(7), 809-817.

[2] Volkow, N.D.; Chang, L.; Wang, G.J.; Fowler, J.S.; Leonido-Yee, M.; Franceschi, D.; Sedler, M.J.; Gatley, S.J.; Hitzemann, R.; Ding, Y.S.; Logan, J.; Wong, C.; Miller, E.N. Association of dopamine transporter reduction with psychomotor impairment in methamphetamine abusers. *Am. J. Psychiatry*, **2001**, *158*(3), 377-382.

[3] Wilson, J.M.; Kalasinsky, K.S.; Levey, A.I.; Bergeron, C.; Reiber, G.; Anthony, R.M.; Schmunk, G.A.; Shannak, K.; Haycock, J.W.; Kish, S.J. Striatal dopamine nerve terminal markers in human, chronic methamphetamine users. *Nat. Med.*, **1996**, *2*(6), 699-703.

[4] Di Chiara, G.; Imperato, A. Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. *Proc. Natl. Acad. Sci. USA,* **1988**, *85*(14), 5274-5278.

[5] Giros, B.; Jaber, M.; Jones, S.R.; Wightman, R.M.; Caron, M.G. Hyperlocomotion and indifference to cocaine and amphetamine in mice lacking the dopamine transporter. *Nature,* **1996**, *379*(6566), 606-612.

[6] Ferre, S.; Fredholm, B.B.; Morelli, M.; Popoli, P.; Fuxe, K. Adenosine-dopamine receptor-receptor interactions as an integrative mechanism in the basal ganglia. *Trends Neurosci.,* **1997**, *20*(10), 482-487.

[7] Ferre, S.; Fuxe, K.; von Euler, G.; Johansson, B.; Fredholm, B.B. Adenosine-dopamine interactions in the brain. *Neuroscience*, **1992**, *51*(3), 501-512.

[8] Gines, S.; Hillion, J.; Torvinen, M.; Le Crom, S.; Casado, V.; Canela, E.I.; Rondin, S.; Lew, J.Y.; Watson, S.; Zoli, M.; Agnati, L.F.; Verniera, P.; Lluis, C.; Ferre, S.; Fuxe, K.; Franco, R. Dopamine D1 and adenosine A1 receptors form functionally interacting heteromeric complexes. *Proc. Natl. Acad. Sci. USA*, **2000**, *97*(15), 8606-8611.

[9] O'Neill, C.; Nolan, B.J.; Macari, A.; O'Boyle, K.M.; O'Connor, J.J. Adenosine A1 receptor-mediated inhibition of dopamine release from rat striatal slices is modulated by D1 dopamine receptors. *Eur. J. Neurosci.*, **2007**, *26*(12), 3421-3428.

[10] Munzar, P.; Justinova, Z.; Kutkat, S.W.; Ferre, S.; Goldberg, S.R. Adenosinergic modulation of the discriminative-stimulus effects of methamphetamine in rats. *Psychopharmacology* (Berl), **2002**, *161*(4), 348-355.

[11] Justinova, Z.; Ferre, S.; Segal, P.N.; Antoniou, K.; Solinas, M.; Pappas, L.A.; Highkin, J.L.; Hockemeyer, J.; Munzar, P.; Goldberg, S.R. Involvement of adenosine A1 and A2A receptors in the adenosinergic modulation of the discriminative-stimulus effects of cocaine and methamphetamine in rats. *J. Pharmacol. Exp. Ther.*, **2003**, *307*(3), 977-986.

[12] Delle Donne, K.T.; Sonsalla, P.K. Protection against methamphetamine-induced neurotoxicity to neostriatal dopaminergic neurons by adenosine receptor activation. *J. Pharmacol. Exp. Ther.*, **1994**, *271*(3), 1320-1326.

[13] Poleszak, E.; Malec, D. Influence of adenosine receptor agonists and antagonists on amphetamine-induced stereotypy in rats. *Pol. J. Pharmacol.*, **2000**, *52*(6), 423-429.

[14] Turgeon, S.M.; Pollack, A.E.; Schusheim, L.; Fink, J.S. Effects of selective adenosine A1 and A2a agonists on amphetamine-induced locomotion and c-Fos in striatum and nucleus accumbens. *Brain Res.*, **1996**, *707*(1), 75-80.

[15] Poleszak, E.; Malec, D. Effects of adenosine receptor agonists and antagonists in amphetamine-induced conditioned place preference test in rats. *Pol. J. Pharmacol.*, **2003**, *55*(3), 319-326.

[16] Ujike, H.; Harano, M.; Inada, T.; Yamada, M.; Komiyama, T.; Sekine, Y.; Sora, I.; Iyo, M.; Katsu, T.; Nomura, A.; Nakata, K.; Ozaki, N. Nine- or fewer repeat alleles in VNTR polymorphism of the dopamine transporter gene is a strong risk factor for prolonged methamphetamine psychosis. *Pharmacogenomics. J*, **2003**, *3*(4), 242-247.

[17] Ren, H.; Stiles, G.L. Separate promoters in the human A1 adenosine receptor gene direct the synthesis of distinct messenger RNAs that regulate receptor abundance. *Mol. Pharmacol.*, **1995**, *48*(6), 975-980.

[18] Ujike, H. Stimulant-induced psychosis and schizophrenia: the role of sensitization. *Curr. Psychiatry Rep.*, **2002**, *4*(3), 177-184.

[19] Schneider, S.; Roessli, D.; Excoffier, L. Arlequin: a software for population genetics data analysis. Version 2.000. Genetics and Biometry Lab, Department of Anthropology, University of Geneva, **2000**.

[20] Deckert, J.; Nothen, M.M.; Albus, M.; Franzek, E.; Rietschel, M.; Ren, H.; Stiles, G.L.; Knapp, M.; Weigelt, B.; Maier, W.; Beckmann, H.; Propping, P. Adenosine A1 receptor and bipolar

affective disorder: systematic screening of the gene and association studies. *Am. J. Med. Genet.*, **1998**, *81*(1), 18-23.

[21] Deckert, J.; Nothen, M.M.; Franke, P.; Delmo, C.; Fritze, J.; Knapp, M.; Maier, W.; Beckmann, H.; Propping, P. Systematic mutation screening and association study of the A1 and A2a adenosine receptor genes in panic disorder suggest a contribution of the A2a gene to the development of disease. *Mol. Psychiatry*, **1998**, *3*(1), 81-85.

[22] Alsene, K.; Deckert, J.; Sand, P.; de Wit, H. Association between A2a receptor gene polymorphisms and caffeine-induced anxiety. *Neuropsychopharmacology*, **2003**, *28*(9), 1694-1702.

[23] Hohoff, C.; McDonald, J.M.; Baune, B.T.; Cook, E.H.; Deckert, J.; de Wit, H. Interindividual variation in anxiety response to amphetamine: possible role for adenosine A2A receptor gene variants. *Am. J. Med. Genet. B Neuropsychiatry. Genet.*, **2005**, *139*B(1), 42-44.

Received: October 01, 2009 Revised: April 17, 2010 Accepted: May 26, 2010