

Hiroyuki Kobayashi, Takahiro Nemoto, Masaaki Murakami, Haruo Kashima, Masafumi Mizuno.	Lack of association between psychosis-like experiences and seeking help from professionals: A case-controlled study.	Schizophrenia Research	132	208-212	2011
Naohisa Tsujino, Takahiro Nemoto, Taiju Yamaguchi, Naoyuki Katagiri, Nao Tohgi, Ryu Ikeda, Nobuyuki Shiraga, Sunao Mizumura, Masafumi Mizuno.	Cerebral blood flow changes in very-late-onset schizophrenia-like psychosis with catatonia before and after successful treatment: a case report.	Psychiatry and Clinical Neurosciences	65	600-603	2011
小林啓之、水野雅文	早期介入による予後改善	精神医学	53	137-142	2011
村上雅昭、水野雅文、藤井千代、Antonio Mastroeni、高橋佳代、稲井友理子	“こころのバリアフリーな街”を目指して 北イタリア地域精神医療最新事情	明治学院大学社会学部附属研究所年報	41	93-105	2011
水野雅文	これからの精神科地域ケアのあり方	臨床精神医学	40	547-550	2011
武士清昭、水野雅文	メンタル面に問題がありそのような患者の診察	診断と治療	99		2011
辻野尚久、水野雅文	統合失調症治療の最前線	ファルマシア	47	829-832	2011
新村秀人、根本隆洋、佐久間啓、水野雅文	地域生活における「幸齢化」をめざして	精神神経学雑誌	113	380-386	2011
水野雅文	サービスモニターの考え方	精神科臨床サービス	11	440-443	2011

Aleksic B, Kushima I, Hashimoto R, Ohi K, Ikeda M, Yoshimi A, Nakamura Y, Ito Y, Okochi T, Fukuo Y, Yasuda Y, Fukumoto M, Yamamori H, Ujike H, Suzuki M, Inada T, Takeda M, Kaibuchi K, Iwata N, Ozaki N	Analysis of the VAV3 as candidate gene for schizophrenia: evidences from voxel based morphometry and mutation screening	Schizophr Bull	39(3)	720-8	2013
Aoki Y, Orikabe L, Takayanagi Y, Yahata N, Mozue Y, Sudo Y, Ishii T, Itokawa M, Suzuki M, Kurachi M, Okazaki Y, Kasai K, Yamasue H	Volume reductions in frontopolar and left perisylvian cortices in methamphetamine induced psychosis	Schizophr Res	147(2-3)	355-61	2013
Miyanishi T, Sumiyoshi T, Higuchi Y, Seo T, Suzuki M	LORETA current source density for duration mismatch negativity and neuropsychological assessment in early schizophrenia	PLoS One	8(4)	e61152	2013
Nakamura K, Takahashi T, Nemoto K, Furuichi A, Nishiyama S, Nakamura Y, Ikeda E, Kido M, Noguchi K, Seto H, Suzuki M	Gray matter changes in high-risk subjects for developing psychosis and first-episode schizophrenia: a voxel-based structural MRI study	Front Psychiatry	18(4)	16.	2013
Takahashi T, Nakamura Y, Nakamura K, Ikeda E, Furuichi A, Kido M, Kawasaki Y, Noguchi K, Seto H, Suzuki M	Altered depth of the olfactory sulcus in first-episode schizophrenia	Prog. Neuropsychopharmacol. Biol. Psychiatry	40(10)	167-72	2013
Takahashi T, Nakamura K, Ikeda E, Furuichi A, Kido M, Nakamura Y, Kawasaki Y, Noguchi K, Seto H, Suzuki M	Longitudinal MRI study of the midline brain regions in first-episode schizophrenia	Psychiatry Res Neuroimaging	212(2)	150-3.	2013

Takahashi T, Nakamura Y, Nakamura K, Nishiyama S, Ikeda E., Furuichi A, Kido M, Noguchi K, Suzuki M	Altered depth of the olfactory sulcus in subjects at risk of psychosis	Schizophr Res	149	186-7	2013
Takahashi T, Nakamura K, Nishiyama S, Furuichi A, Ikeda E, Kido M, Nakamura Y, Kawasaki Y, Noguchi K, Seto H, Suzuki M	Increased pituitary volume in early psychosis	Psychiatry Clin Neurosci	67(7)	540-8	2013
Takayanagi M, Wentz J, Takayanagi Y, Schretlen DJ, Ceyhan E, Wang L, Suzuki M, Sawa A, Barta PE, Ratnanather JT, Cascella NG	Reduced anterior cingulate gray matter volume and thickness in subjects with deficit schizophrenia	Schizophr Res	150	484-90	2013
Nakamura K, Kawasaki Y, Takahashi T, Furuichi A, Noguchi K, Seto H, Suzuki M	Reduced white matter fractional anisotropy and clinical symptoms in schizophrenia: a voxel-based diffusion tensor imaging study	Psychiatry Research Neuroimaging	202	233-238	2012
Kushima I, Aleksic B, Ito Y, Nakamura Y, Shiino T, Okochi T, Fukuo Y, Ujike H, Suzuki M, Inada T, Hashimoto R, Takeda M, Kaibuchi K, Iwata N, Ozaki N	Resequencing and association analysis of the KALRN and EPHB1 genes and their contribution to schizophrenia susceptibility	Schizophrenia Bulletin	38	552-560	2012
Uematsu A, Matsui M, Tanaka C, Takahashi T, Noguchi K, Suzuki M, Nishijo H	Developmental trajectories of amygdala and hippocampus from infancy to early adulthood in healthy individuals	PLoS ONE	7	e46970	2012

Takahashi T, Kidō M, Nakamura K, Furuichi A, Zhou S-Y, Kawasaki Y, Noguchi K, Seto H, Kurachi M, Suzuki M	Longitudinal MRI study of the pituitary volume in chronic schizophrenia: a preliminary report	Psychiatry Research Neuroimaging	202	84-87	2012
Koide T, Aleksic B, Banno M, Yamashita S, Kikuchi T, Kohmura K, Adachi Y, Kawano N, Kushima I, Nakamura Y, Ikeda M, Ohi K, Yasuda Y, Hashimoto R, Inada T, Ujike H, Iidaka T, Suzuki M, Takeda M, Iwata N, Ozaki N	Common variants in MAGI2 gene are associated with increased risk for cognitive impairment in schizophrenic patients	PLoS ONE	7	e36836	2012
Ikeda M., Aleksic B., Kinoshita Y., Okochi T., Kawashima K., Kushima I., Ito Y., Nakamura Y., Kishi T., Okumura T., Fukuo Y., Williams H.J., Hamshere M.L., Ivanov D., Inada T., Suzuki M., Hashimoto R., Ujike H., Takeda T., Craddock N., Kaibuchi K., Owen M.J., Ozaki N., O'Donovan M.C., and Iwata N	Genome-wide association study of schizophrenia in a Japanese population	Biol. Psychiatry	69	472-478	2011
Itoh T., Sumiyoshi T., Higuchi Y., Suzuki M., and Kawasaki Y	LORETA analysis of three-dimensional distribution of delta-band activity in schizophrenia: Relation to negative symptoms	Neurosci. Res	70	442-8	2011

Orikabe L., Yamasue H., Inoue H., Takayanagi Y., Mozue Y., Sudo Y., Ishii T., Itokawa M., Suzuki M., Kurachi M., Okazaki Y., and Kasai K	Reduced amygdala and hippocampal volumes in patients with methamphetamine psychosis	Schizophr. Res	132	183-189	2011
Takahashi T., Zhou S.Y., Nakamura K., Tanino R., Furuichi A., Kido M., Kawasaki Y., Noguchi K., Seto H., Kurachi M., and Suzuki M	Longitudinal volume changes of the pituitary gland in patients with schizotypal disorder and first-episode schizophrenia	Prog. Neuropsychopharmacol. Biol. Psychiatry,	35	177-183	2011
Takahashi T., Zhou S.Y., Nakamura K., Tanino R., Furuichi A., Kido M., Kawasaki Y., Noguchi K., Seto H., Kurachi M., and Suzuki M	A follow-up MRI study of the fusiform gyrus and middle and inferior temporal gyri in schizophrenia spectrum	Prog. Neuropsychopharmacol. Biol. Psychiatry	35	1957-1964	2011
Takayanagi Y., Takahashi T., Orikabe L., Mozue Y., Kawasaki Y., Nakamura K., Sato Y., Itokawa M., Yamasue H., Kasai K., Kurachi M., Okazaki Y., and Suzuki M	Classification of first-episode schizophrenia patients and healthy subjects by automated MRI measures of regional brain volume and cortical thickness	PLoS ONE	6	e21047	2011
鈴木道雄, 高橋 努	統合失調症と脳の形態変化	日本臨床	71	619-623	2013
住吉太幹, 西山志満子, 樋口悠子, 高橋 努, 松岡 理, 倉知正佳, 水上祐子, 数川 悟, 鈴木道雄	富山県における早期介入活動の実際と工夫	精神神経学雑誌	115	180-186	2013
高橋 努, 鈴木道雄	統合失調症圏の MRI 研究の進歩	精神神経学雑誌	115	874-879	2013
川崎康弘, 鈴木道雄	統合失調症を脳画像で診断するための VBM	日本磁気共鳴医学会雑誌	32	41-47	2012

高橋 努, 中村主計, 鈴木道雄	アットリスク精神状態の MRI 研究	臨床精神医学	41	1421-142 6	2012
中村主計, 高橋 努, 鈴木道雄	早期統合失調症と脳の形態 変化	精神科治療学	26	1421-142 6	2011
鈴木道雄	統合失調症の早期介入と脳 画像診断	日本精神科病院 協会雑誌	29	35-40	2011
鈴木道雄, 高橋 努, 川崎康弘, 中村主計, 高柳陽一郎	統合失調症における脳の構 造画像マーカー	精神科	18	506-512	2011
高橋 努, 鈴木道雄	早期精神病における脳形態 変化	日本生物学的精 神医学会誌	22	15-20	2011
Watanabe N, Furukawa TA, Shimodera S, Katsuki F, Fujita H, Sasaki M, Suga Y, Kakeda K, Perlis ML.	Can assessors in a psychotherapy trial be successfully blinded? Analysis of a randomized controlled trial on psychotherapy for refractory insomnia in residual depression.	Psychother Psychosom	82(6)	401-403	2013
Morokuma I, Shimodera S, Fujita H, Hashizume H, Kamimura N, Kawamura A, Nishida A, Furukawa TA, Inoue S.	Psychoeducation for major depressive disorders: a randomised controlled trial.	Psychiatry Res	30;210(1)	134-139	2013
Kinoshita M, Numata S, Tajima A, Shimodera S, Imoto I, Ohmori T	Plasma total homocysteine is associated with DNA methylation in patients with schizophrenia.	Epigenetics	8(6)	584-590	2013
Ando S, Yamasaki S, Shimodera S, Sasaki T, Oshima N, Furukawa TA, Astukai N, Kasai K, Mino Y, Inoue S, Okazaki Y, Nishida A	A greater number of somatic pain sites is associated with poor mental health in adolescents: a cross-sectional study.	BMC Psychiatry	17	13-30	2013

Kinoshita M, Numata S, Tajima A, Shimodera S, Ono S, Imamura A, Iga J, Watanabe S, Kikuchi K, Kubo H, Nakataki M, Sumitani S, Imoto I, Okazaki Y, Ohmori T.	DNA methylation signatures of peripheral leukocytes in schizophrenia.	Neuromolecular r Med	15(1)	95-101	2013
Ikeda M, Aleksic B, Yamada K, Iwayama-Shigeno Y, Matsuo K, Numata S, Watanabe Y, Ohnuma T, Kaneko T, Fukuo Y, Okochi T, Toyota T, Hattori E, Shimodera S, Itakura M, Nunokawa A, Shibata N, Tanaka H, Yoneda H, Arai H, Someya T, Ohmori T, Yoshikawa T, Ozaki N, Iwata N.	Genetic evidence for association between NOTCH4 and schizophrenia supported by a GWAS follow-up study in a Japanese population.	Mol Psychiatry	18(6)	636-638	2013
Tochigi M, Nishida A, Shimodera S, Okazaki Y, Sasaki T	Season of birth effect on psychotic-like experiences in Japanese adolescents.	Eur Child Adolesc Psychiatry	22(2)	89-93	2013
Shimodera S, Imai Y, Kamimura N, Morokuma I, Fujita H, Inoue S, Furukawa TA	Near-infrared spectroscopy(NIRS) of bipolar disorder may be distinct from that of unipolar depression and of healthy controls.	Asia-Pac Psychiatry	4(4)	258-265	2012
Furukawa TA, Watanabe N, Kinoshita Y, Kinoshita K, Sasaki T, Nishida A, Okazaki Y, Shimodera S	Public speaking fears and their correlates among 17,615 Japanese adolescents.	Asia-Pac Psychiatry	Apr;11	1758-587 2	2012

Watanabe N, Nishida A, Shimodera S, Inoue K, Oshima N, Sasaki T, Inoue S, Akechi T, Furukawa TA, Okazaki Y	Help seeking behaviors among Japanese school students who self-harm; results from a self-report survey with 18,104 adolescents.	Neuropsychiatr Dis Treat	8	561-569	2012
An SK, Chan SK, Chang WC, Chend EY, Chong SA, Chung YC, Hui CL, Hwu HG, Iwata N, Irmansyah I, Jang JH, Kwon JS, Lee JC, Lee HM, Lee EH, Li T, Liu Z, Ma X, Mangala R, Marchira C, Matsumoto K, Mizuno M, Shimodera S, Subandi MA, Suzuki M, Tay SA, Thara R, Verma SK, Wong GH	Early psychosis declaration for Asia by the Asian network of early psychosis.	East Asian Arch Psychiatry	22	90-93	2012
Shimodera S, Yonekura Y, Yamaguchi S, Kawamura A, Mizuno M, Inoue S, Furukawa TA, Mino Y	Bipolar I disorder and expressed emotion of families; a cohort study in Japan.	OJPsych	2	258-261	2012
Tochigi M, Nishida A, Shimodera S, Oshima N, Inoue K, Okazaki Y, Sasaki T	Irregular bedtime and nocturnal cellular phone usage as risk factors for being involved in bullying; a cross-sectional survey of Japanese adolescents.	PLoS ONE	7(9)	1-6	2012
Kinoshita M, Numata S, Tajima A, Ohi K, Hashimoto R, Shimodera S, Imoto I, Itakura M, Takeda M, Ohmori T	Meta-analysis of association studies between DISC1 missense variants and schizophrenia in the Japanese population.	Schizophr Res	141	271-273	2012

Kubo T, Sato T, Noguchi T, Kitaoka H, Yamasaki F, Kamimura N, Shimodera S, Iiyama T, Kumagai N, Kakinuma Y, Diedrich A, Jordan J, Robertson D, Doi YL	Influences of donepezil on cardiovascular system - possible therapeutic benefits for heart failure - DOnepezil Cardiac TEst Registry(DOCTER) study		60(3)	310-314	2012
Shimodera S, Kato T, Sato H, Miki K, Shinagawa Y, Kondo M, Fujita H, Morokuma I, Ikeda Y, Akechi T, Watanabe N, Yamada M, Inagaki M, Yonemoto N, Furukawa TA	The first 100 patients in the SUN-D trial(strategic use of new generation antidepressants for depression); examination of feasibility and adherence during the pilot phase	Trials	13(80)	1-11	2012
Watanabe N & Nishida A, Shimodera S, Inoue K, Oshima N, Sasaki T, Inoue S, Akechi T, Furukawa TA, Okazaki Y	Deliberate self-harm in adolescents aged 12 - 18; a cross-sectional survey of 18,104 students.	Suicide Life Threat Behav	42(5)	550-560	2012
Kinoshita K, Kinoshita Y, Shimodera S, Nishida A, Inoue K, Watanabe N, Oshima N, Akechi T, Sasaki T, Inoue S, Furukawa TA, Okazaki Y	Not only body weight perception but also body mass index is relevant to suicidal ideation and self-harming behavior in Japanese adolescents.		200(4)	305-309	2012
Oshima N, Nishida A, Shimodera S, Tochigi M, Ando S, Yamasaki S, Okazaki Y, Sasaki T	The suicidal feelings, self-injury, and mobile phone use after lights out in adolescents	J Pediatr Psychol	37(9)	1023-1030	2012

Ikeda M, Aleksic B, Yamada K, Iwayama-Shigeno Y, Matsuo K, Numata S, Watanabe Y, Ohnuma T, Kaneko T, Fukuo Y, Okochi T, Toyota T, Hattori E, Shimodera S, Itakura M, Nunokawa A, Shibata N, Tanaka H, Yoneda H, Arai H, Someya T, Ohmori T, Yoshikawa T, Ozaki N, Iwata N	Genetic evidence for association between NOTCH4 and schizophrenia supported by a GWAS follow-up study in a Japanese population.	Mol Psychiatr	1-2	1-8	2012
Shimodera S, Furukawa TA, Mino Y, Shimazu K, Nishida A, Inoue S	Cost-effectiveness of family psychoeducation to prevent relapse in major depression; results from a randomized controlled trial.	BMC Psychiatry	12(40)	1-6	2012
Shimodera S, Imai Y, Kamimura N, Morokuma I, Fujita H, Inoue S, Furukawa TA	Mapping hypofrontality during letter fluency task in schizophrenia: a multi-channel near-infrared spectroscopy study	Schizophr Res	136	63-69	2012
Shimodera S, Kawamura A, Furukawa TA	Physical pain associated with depression: results of a survey in Japanese patients and physicians.	Compr Psychiat	53	843-849	2012
Lihong Q, Shimodera S, Fujita H, Morokuma I, Nishida A, Kamimura N, Mizuno M, Furukawa TA, Inoue S	Duration of untreated psychosis in a rural/suburban region of Japan.	Early Interv Psychiatry	6	239-246	2012
Shimodera S	Author's reply to Bichitra N.Patra.	Br J Psychiatry	200	82-83	2012

下寺信次, 井上新平, 藤田博一, 須賀楓介	アーリーサイコーシス外来 における早期介入	精神神経学雑誌	115(2)	168-173	2013
下寺信次, 井上新平, 藤田博一, 須賀楓介	我が国における統合失調症 早期介入の現状	第 108 回日本精 神神経学会学術 総会特集号 (電 子版)		SS33-SS3 8	2013
藤田博一, 下寺信次	認知・行動療法と家族療法 の併用と治療効果	臨床精神医学	41(8)	1017-102 2	2012
下寺信次	思春期の精神障害の疫学と 精神疾患の早期介入	精神科治療学	26(6)	677-680	2011
下寺信次, 藤田博一, 河村葵	うつ病の心理教育ポイント とコツ	Medical Practice	28(10)	1827-183 0	2011
上村直人, 福島章恵, 弘田りさ, 今城由里 子, 下寺信次	高齢者・認知症と性的問題 行動	精神科	19(2)	192-197	2011
下寺信次	統合失調症の家族心理教 育; 現場でいかに実践する か	認知療法研究	4(2)	111-118	2011
Fumiaki Ito, Kazunori Matsumoto, Tetsuo Miyakoshi, Noriyuk i Ohmuro, Tomohiro Uchida, Hiroo Matsuoka	Emotional processing during speech communication and positive symptoms in schizophrenia	Psychiatry and Clinical Neurosciences	67	526-531	2013
大野高志, 舩越俊一, 角藤芳久, 谷口宏, 高松杏子, 野村綾, 横川信弘, 齋藤和子, 香山明美, 石黒奈々 子, 大室則幸, 桂雅 宏, 濱家由美子, 小 高晃, 松本和紀, 松 岡洋夫	名取 EI プロジェクト-宮 城県立精神医療センターを 中心とした早期介入プロジ ェクトについて-	精神神経学雑誌	115 (2)	147-153	2013

松本和紀、濱家由美子、光永憲香、内田知宏、砂川恵美、大室則幸、桂雅宏、松岡洋夫	サイコーシス早期段階における CBT の活用	精神神経学雑誌	115 (4)	390-398	2013
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	精神経誌	114 (3)	303-309	2012
松岡洋夫	統合失調症顕在発症前のハイリスク状態	児童青年精神医学とその近接領域	53	423-429	2012
内田知宏、川村知慧子、三船奈緒子、濱家由美子、松本和紀、安保英勇、上埜高志	日本版 Brief Core Schema Scale を用いた自己、他者スキーマの検討—クラスターパターンの類型化および抑うつとの関連	パーソナリティ研究	20	143-154	2012
桂雅宏、小原千佳、松本和紀	精神病アットリスク状態 (ARMS) に対する早期介入	臨床精神医学	41 (10)	1413-1419	2012
Takeshi Nakano, Shinji Ono, Junji Yamaguchi, Ryu Sugimoto, Naohiro Yamaguchi, Yoshiro Morimoto, Tatsuya Kubo, Hiroki Ozawa, Naohiro Kurotaki	Modified electroconvulsive therapy for the treatment of refractory schizophrenia-like psychosis associated with Huntington's disease	J Neurol.	260.	312-314	2013
野中俊輔, 一ノ瀬仁志, 木下裕久, 中根秀之	一般住民、医療従事者への精神障害に対する啓発活動およびアンチスティグマ研究	臨床精神医学	41 (10)	1439-1446	2013
野中俊輔, 一ノ瀬仁志, 木下裕久, 中根秀之	統合失調症の疫学	日本臨床	71 (4)	583-588	2013
今村明, 小野慎治, 辻田高弘, 橋田あおい, 黒滝直弘, 小澤寛樹, 岡崎祐士	一卵性双生児精神疾患一一致例におけるコピー数解析	日本生物学的精神医学会誌	23(1)	23-28	2012
野中俊輔, 一ノ瀬仁志, 木下裕久, 中根秀之	一般住民、医療従事者への精神障害に対する啓発活動およびアンチスティグマ研究	臨床精神医学	41 (10)	1439-1446	2012

小野慎治, 黒滝直弘, 木下裕久, 小澤寛樹, 今村明	【脳の機能と統合失調症・ 新たな診断と治療への展望 -I】 コピー数変異と統合失 調症	精神科治療学	26 (11)	1387-139 3	2011
木下裕久, 野畑宏之, 野中俊輔, 久保達 哉, 磨井章智, 黒滝 直弘, 小澤寛樹,	初発統合失調症患者に対す るクエチアピン単剤の有用 性 至適用量を考慮して	新薬と臨床	60 (12)	2476-248 2	2011
田山達之, 渡邊尚子, 木下裕久, 金替伸治, 黒滝直弘, 小澤寛樹	【症状性を含む器質性精神 障害の症例】 関節リウマチ に対し投与した抗 IL-6 受 容体抗体が精神病症状の出 現に関与したと考えられた 1 症例	臨床精神医学	40 (10)	1387-139 0	2011
太田豊作, 飯田順三, 石川翠里, 岸本直子, 島本卓也, 岸本年史	他院で At-Risk Mental State と診断され、当科で 身体醜形障害と診断した一 例	最新精神医学	18 (3)	1342-430 0	2013
松岡究, 芳野浩樹, 江浦信之, 盛本翼, 太田豊作, 橋本和典, 上野聡, 岸本年史	短期間に再発した抗 NMDA 受容体脳炎の男性 例	精神医学	55 (6)	561-564	2013
後藤晴栄, 安野史彦, 小坂淳, 岡田光司, 岸本年史	悪性腫瘍における終末期の 精神的苦痛に関して回想法 が有効であった統合失調症 の一例	精神科	23 (3)	376-380	2013
Ota T, Iida J, Sawada M, Suehiro Y, Kishimoto N, Tanaka S, Nagauchi K, Nakanishi Y, Yamamuro K, Negoro H, Iwasaka H, Sadamatsu M, Kishimoto T.	Comparison of pervasive developmental disorder and schizophrenia by the Japanese version of the National Adult Reading Test.	International Journal of Psychiatry in Clinical Practice.	17(1)	10-15	2012
橋本和典, 岸本年史	統合失調症と喫煙	日本社会精神医 学会雑誌	21 (1)	89-93	2012
岸本年史	統合失調症 過去・現在・ 未来	日本社会精神医 学会雑誌	21 (1)	84-88	2012
太田豊作, 飯田順三, 岸本年史	成人の広汎性発達障害にお ける補助診断ツールの意義	精神神経学雑誌	113 (11)	1137-114 4	2011

澤田将幸, 飯田順三, 根來秀樹, 太田豊作, 岸本年史	発達障害の事象関連電位と NIRS	児童青年精神医 学とその近接領 域	52 (4)	417-420	2011
M Ikeda, B Aleksic, Y Kinoshita, T Okochi, K Kawashima, I Kushima, Y Ito, Y Nakamura, T Kishi, T Okumura, Y Fukuo, HJ Williams, ML Hamshere, D Ivanov, T Inada, M Suzuki, R Hashimoto, H Ujike, M Takeda, N Craddock, K Kaibuchi, MJ Owen, N Ozaki, MC O'Donovan, and N Iwata	Genome-wide association study of schizophrenia in a Japanese population.	Biological psychiatry	69(5)	472-8	2011
Kajio Y, Kondo K, Saito T, Iwayama Y, Aleksic B, Yamada K, Toyota T, Hattori E, Ujike H, Inada T, Kunugi H, Kato T, Yoshikawa T, Ozaki N, Ikeda M and Iwata N	Genetic association study between the detected risk variants based upon type II diabetes GWAS and psychotic disorders in the Japanese population	Journal of human genetics		In press	2013
Ikeda M, Okahisa Y, Aleksic B, Won M, Kondo N, Naruse N, Aoyama-Uehara K, Sora I, Iyo M, Hashimoto R, Kawamura Y, Nishida N, Miyagawa T, Takeda M, Sasaki T, Tokunaga K, Ozaki N, Ujike H and Iwata N	Evidence for shared genetic risk between methamphetamine-induc ed psychosis and schizophrenia	Neuropsychoph armacology	38(10)	1864-70	2013

Kondo K, Ikeda M, Kajio Y, Saito T, Iwayama Y, Aleksic B, Yamada K, Toyota T, Hattori E, Ujike H, Inada T, Kunugi H, Kato T, Yoshikawa T, Ozaki N and Iwata N	Genetic variants on 3q21 and in the Sp8 transcription factor gene (SP8) as susceptibility loci for psychotic disorders: a genetic association study	PLoS One	8(8)	e70964	2013
Kanazawa T, Ikeda M, Glatt SJ, Tsutsumi A, Kikuyama H, Kawamura Y, Nishida N, Miyagawa T, Hashimoto R, Takeda M, Sasaki T, Tokunaga K, Koh J, Iwata N and Yoneda H	Genome-wide association study of atypical psychosis	American journal of medical genetics	162B(7)	679-86	2013
M Ikeda, B Aleksic, K Yamada, Y Iwayama-Shigeno, K Matsuo, S Numata, Y Watanabe, T Ohnuma, T Kaneko, Y Fukuo, T Okochi, T Toyota, E Hattori, S Shimodera, M Itakura, A Nunokawa, N Shibata, H Tanaka, H Yoneda, H Arai, T Someya, T Ohmori, T Yoshikawa, N Ozaki and N Iwata	Genetic evidence for association between NOTCH4 and Schizophrenia supported by a GWAS follow-up study in a Japanese population	Mol Psychiatry	18(6)	636-8	2013
古橋功一、岩田仲生	Ⅲ. 統合失調症の臨床 統合失調症の薬物療法「各病期における治療目標と薬物療法」	日本臨牀	第 71 卷・第 4 号	635-640	2013 年 4 月

Takahashi T, Nakamura K, Ikeda E, Furuichi A, Kido M, Nakamura Y, Kawasaki Y, Noguchi K, Seto H, Suzuki M.	Longitudinal MRI study of the midline brain regions in first-episode schizophrenia.	Psychiatry Res	212	150-153	2013
Higuchi Y, Sumiyoshi T, Seo T, Miyanishi T, Kawasaki Y, Suzuki M.	Mismatch negativity and cognitive performance for the prediction of psychosis in subjects with at-risk mental state.	PLoS One	8	e54080	2012
Takahashi T, Nakamura Y, Nakamura K, Ikeda E, Furuichi A, Kido M, Kawasaki Y, Noguchi K, Seto H, Suzuki M.	Altered depth of the olfactory sulcus in first-episode schizophrenia.	Prog Neuropsychopharmacol Biol Psychiatry	40	167-172	2012
Nakamura K, Kawasaki Y, Takahashi T, Furuichi A, Noguchi K, Seto H, Suzuki M.	Reduced white matter fractional anisotropy and clinical symptoms in schizophrenia: a voxel-based diffusion tensor imaging study.	Psychiatry Res	202	233-238	2012
Takahashi T, Kido M, Nakamura K, Furuichi A, Zhou SY, Kawasaki Y, Noguchi K, Seto H, Kurachi M, Suzuki M.	Longitudinal MRI study of the pituitary volume in chronic schizophrenia: a preliminary report.	Psychiatry Res	202	84-87	2012
新田佑輔	統合失調症患者における Design fluency test による前頭葉の賦活 : NIRS 研究.	金医大誌	38	1-8	2013
鈴木道雄, 川崎康弘, 高柳陽一郎, 中村主計, 高橋 努	構造MRI による統合失調症の補助診断の可能性.	精神神経科学雑誌	114	807-810	2012
川崎康弘	統合失調症を脳画像で診断するためのVBM.	日磁医誌	32	41-46	2012

IV. 研究成果の刊行物・別刷



Original Article

Poor outcome associated with symptomatic deterioration among help-seeking individuals at risk for psychosis: a naturalistic follow-up study

Keiko Morita,¹ Hiroyuki Kobayashi,² Kiyooki Takeshi,¹ Naohisa Tsujino,¹ Takahiro Nemoto¹ and Masafumi Mizuno¹

Abstract

Aims: It remains debatable whether early intervention for psychosis is capable of meeting the needs of at-risk subjects. The aims of this study were to describe the actual impact of interventions on subjective difficulties and to explore the factors that may be associated with a poor outcome.

Methods: Participants were help-seeking outpatients at a university hospital who met the Criteria of Prodromal Syndromes. Changes in the symptoms, subjective experience and current insight were assessed using the Scales of Prodromal Symptoms, the Subjective Well-being under Neuroleptics, and the Scale to Assess Unawareness of Mental Disorder, respectively. Global functioning, social functioning and subjective quality of life were evaluated using the Global Assessment of Functioning

Scale, the Social Functioning Scale, and the WHO-Quality of Life 26, respectively. These measures were assessed both at baseline and after 1 year.

Results: Forty-six patients agreed to participate. Of the 27 patients who completed the reassessment at the follow-up point, 13 patients (48%) showed little improvement in their positive/negative symptoms, subjective well-being or awareness of their symptoms. Additionally, less severe negative symptoms, more severe general symptoms and lower subjective well-being at baseline significantly predicted a deterioration of positive/negative symptoms after 1 year.

Conclusion: Our findings suggest that the current strategy for reducing psychosis risk based on positive symptoms should be reappraised.

¹Department of Neuropsychiatry, School of Medicine, Toho University, Tokyo, Japan; and ²Department of Psychiatry, University of Cambridge, Cambridge, UK

Corresponding author: Dr. Hiroyuki Kobayashi, Department of Psychiatry, University of Cambridge, Box 189, Level 4, Addenbrooke's Hospital Hills Road, Cambridge CB2 2QQ, UK. Email: hiro.yuki.kob@gmail.com

Received 15 May 2012; accepted 30 September 2012

Key words: at-risk mental states, early intervention, prodrome, psychosis, quality of life.

INTRODUCTION

In the last 15 years, a number of studies have supported the view that the earlier detection and care of psychosis can lead to a better outcome.^{1,2} However, most of these studies were conducted in research settings; thus, the actual *effectiveness* of early intervention for psychosis remains unclear.³ One of the issues that such studies have raised is that the diagnostic criteria or primary outcomes focus mainly on the attenuated positive psychotic symptoms.

Attenuated psychotic symptoms or psychotic-like experiences have been commonly found in the

general population, and these symptoms or experiences may not necessarily be associated with distress or help-seeking behaviour.^{4–6} In a previous study comparing help-seeking patients with the general population, the authors reported that psychosis-like experiences do not significantly contribute to help-seeking behaviour.⁷ Attenuated positive symptoms may not always confer subjective difficulties or sufferings; therefore, the current interventions to reduce risk which are focused on the attenuated positive symptoms may not be truly capable of meeting the needs of individuals meeting at-risk criteria.

Poor outcome among at-risk patients

To date, longitudinal studies on the outcomes of individuals at risk for psychosis have underlined the considerably high rates of remission⁸ and the low rates of transition to psychosis.^{9,10} Given that the criteria for remission and transition are based on the attenuated psychotic symptoms, however, it would be doubtful whether or not these outcomes reflect the actual changes in subjective difficulties of individuals at risk for psychosis. Indeed, a large longitudinal study, the North American Prodrome Longitudinal Study (NAPLS), revealed that most individuals who met the at-risk criteria but did not convert to psychosis continued to suffer from lower levels of functioning or disabilities.¹¹ Additionally, an approach focused predominantly on the low rate of transition to psychotic disorder can obscure individual treatment effects. Subgroups of participants may respond to individual treatments particularly well or particularly poorly as a result of the participants' characteristics or baseline symptom patterns. A recent report on a randomized controlled trial examining the effect of various therapies on young people with a high risk for psychosis concluded that the interventions were equally effective or ineffective.¹² Thus, the *effectiveness* of interventions for early psychosis should be clarified in clinical settings, regardless of the transition to full-blown psychosis.

We hypothesized that the current strategy, which is focused on the attenuated positive symptoms, cannot sufficiently ameliorate the subjective difficulties of individuals at risk for psychosis, such as their subjective quality of life (QOL), role/social functioning, interpersonal relationships and subjective well-being. We also assumed that some patients would continue to receive treatment because their symptoms had not been relieved.

The aims of this study were: (i) to describe the actual 1-year outcome of individuals with a high risk of psychosis based on comprehensive assessments including subjective QOL, role/social functioning, interpersonal relationships, insight into illness and subjective well-being; and (ii) to clarify the characteristics of patients who continue to receive treatment for over 1 year so as to explore the factors that may lead to a poor outcome, even without a transition to psychosis.

METHODS

Participants

This study was performed at a university hospital (Toho University) located in a suburb of Tokyo. The participants were eligible for enrolment in the study if they were between the ages of 16 and 40 years and

met the Criteria of Prodromal Syndromes (COPS).¹³ Patients were excluded from the study if they had: (i) any lifetime DSM IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) diagnosis of any psychotic disorder; (ii) symptoms fully accounted for by an Axis I disorder or sequelae arising from drug/alcohol use; or (iii) abuse of alcohol or drugs. All the participants were help-seeking outpatients. Each adult participant provided his or her written informed consent and each minor provided written informed assent in addition to consent from a parent or guardian. Data were collected between June 2007 and October 2009.

Measures

The Structured Interview for Prodromal Syndromes (SIPS)¹³ was performed for patients identified as having an 'at-risk mental state', including the Scale of Prodromal Symptoms (SOPS). The SOPS items consist of four symptoms: positive symptoms, negative symptoms, disorganized symptoms, and general symptoms, although the COPS focuses upon merely positive symptoms. We used the SIPS/SOPS Japanese version, which we previously reported to have an excellent interrater reliability.¹⁴ The developers of this SIPS/SOPS Japanese version (H. Kobayashi and M. Mizuno) trained the staff to score these tests with accuracy, and the interviews (including the SIPS and the other assessments) were conducted by experienced psychiatrists (K. Morita, K. Takeshi and N. Tsujino).

Changes in subjective experience were assessed using the Subjective Well-being under Neuroleptics Short version (SWNS).¹⁵ The SWNS is a 20-item test that uses a 6-point Likert-type self-rating scale. Naber *et al.* found a five-factor solution for the scale, which was interpreted as emotional regulation, self-control, mental functioning, social integration and physical functioning. We used the SWNS Japanese version, which has been shown to have a good reliability and validity.¹⁶

Current insight was measured using the Scale to Assess Unawareness of Mental Disorder (SUMD).¹⁷ The SUMD rates awareness of 20 items was based on a 5-point Likert scale. To assess current insight, we used the 3 global insight items (awareness of mental disorder, awareness of achieved medication effects, and awareness of social consequences of medications) and the 17 subscales (awareness of symptoms).

Global functioning, social functioning and subjective QOL were evaluated using the Global Assessment of Functioning Scale, the Social Functioning Scale, and the WHO-Quality of Life 26, respectively.

These measures were assessed both at baseline and after 1 year. The Institutional Review Board at Toho University approved the study protocol and the procedure for obtaining informed consent.

Interventions

During the follow-up period, all the patients received usual supportive therapy and/or psychotropic medication, with the main aim of reducing the severity of psychotic symptoms. Psychotropic medication included the use of antipsychotics for positive symptoms, anxiolytics for anxiety symptoms, and antidepressants for comorbid depressive symptoms, if necessary. The administration of antipsychotics was generally judged according to the International Clinical Practice Guidelines for Early Psychosis.¹⁸ The nature of the psychological intervention was left to the discretion of the psychiatrist in charge; cognitive therapy, psychoeducation, or family therapy, if used, were thus provided in diverse forms.

Clinical outcome

To determine the factors that may lead to a poor outcome, even without a transition to psychosis, the sample was subsequently split into two groups according to the degree to which either positive or negative symptoms had developed. At the follow-up point, patients with improvements from the baseline in both the SOPS positive and negative symptom scores without transitioning to psychosis were defined as 'improved', and patients with no improvements from the baseline in the SOPS positive or negative symptoms or who fulfilled the criteria for psychosis were defined as 'not improved'. The transition to psychosis was operationally defined using the Presence of Psychotic Symptoms criteria.¹³

Statistical analyses

All the statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). The baseline variables were compared between the patients who were lost because of attrition and the patients who were followed up after 1 year with the help of Mann-Whitney *U*-tests for continuous variables and with chi-square tests for categorical variables. Also, clinical variables at baseline were compared between the 'improved' group and the 'not improved' group using the Mann-Whitney *U*-tests for continuous variables and the chi-square tests for categorical variables. In addition, we com-

pared clinical outcomes between the 'improved' group and the 'not improved' group using the analysis of variance, adjusting for age, duration of illness and baseline scores. To explore variables that can predict poor outcomes, multiple linear regression analysis was conducted. For each comparison, a value of $P < 0.05$ was considered statistically significant without any consideration for multiple comparisons.

RESULTS

At baseline, 46 treatment-seeking patients who had been clinically diagnosed as having clinical high risk of psychosis agreed to participate in the study and to be assessed. The demographic characteristics of the sample at baseline are presented in Table 1.

At the 1-year follow-up point, 27 participants (59%) completed the reassessment. Table 2 shows the sample characteristics of these 27 patients and the patients who withdrew from the study, indicating that the withdrawn patients were younger and had a shorter duration of illness, less negative/general symptoms and a higher QOL.

During the follow-up period, three patients, or 12% of the followed sample, converted to psychosis: two were diagnosed as having schizophrenia and one was diagnosed as having a schizoaffective disorder. According to the criteria mentioned above, 14 patients were defined as 'improved' (in both the SOPS positive and negative symptoms), but 13 patients, including the 3 psychotic cases, were defined as 'not improved' (in either the SOPS positive or negative symptoms). Detailed comparisons of these two groups are shown in Table 3, suggesting that although few differences in the clinical variables were found between the two groups at baseline, all the patients in the 'not improved' group had past treatment histories and had fewer family members with mental health illness.

Table 4 shows that 'not improved' group demonstrated a decline of the SWNS total score and the SUMD sub-score (awareness of symptoms) over time, even after adjusting for age, duration of illness and baseline scores. Twenty-one (78% of the followed) patients had received antipsychotic medication at the follow-up point (aripiprazole: $n = 13$; quetiapine: $n = 5$; perospirone: $n = 2$; risperidone: $n = 1$), whereas only six patients (22%) were administered antipsychotic treatment at baseline (quetiapine: $n = 2$; risperidone: $n = 2$; aripiprazole: $n = 1$; perospirone: $n = 1$) (Table 3).

Multiple linear regression analysis was used to explore variables at baseline that can predict poorer