

精神病発前駆期に認められる主観的および客観的な神経心理学的異常

Hambrecht M et al: Subjective and objective neuropsychological abnormalities in a psychosis prodrome. Br J Psychiatry Suppl 43: s30-37, 2002.

#### 対象

前駆期の被験者 51 名（年齢 25.5±6 歳、男性 42 名、女性 9 名）、統合失調症 29 名（年齢 22.97±3.81 歳、男性 22 名、女性 7 名）、健常対照 29 名（年齢 23.97±3.04 歳、男性 22 名、女性 7 名）。前駆期の被験者はドイツで最初の早期発見センターである FETZ (FrühErkennungs- und Therapie-Zentrum für Psychische Krisen)の利用者。FETZはColonge大学病院内に精神科とは独立して設置され、定期的なニュースレター、セミナーや、早期発見週間、ホームページ、ラジオ、テレビなどで啓蒙し10ヶ月間で250件の電話相談、120件を超える専門機関からの照会によって158名が来所した。これらから9項目の基準のうち2項目以上を認めたものを前駆期対象者とした。基準項目はDSM-III-Rの前駆期項目とKlosterkötterら(2001)の基底症状から採用した。基底症状はBSABS (Bonn Scale for the Assessment of Basic Symptoms)を用いて評価した。

#### 方法

CPT (continuous performance test), DRT (delayed response test), AVLT (auditory verbal learning test), 言語流暢性試験 (verbal fluency test), Rey-Osterrieth 複合図表試験, WCST を用いて神経心理学的評価を前駆期、統合失調症、健常対照の間で比較検討した。

#### 結果と考察

51名の前駆期被験者は15ヶ月間のフォローアップ中に5例が統合失調症を顕在発症した。BSABSの項目では集中困難、日常の社会的出来事への耐性低下、視覚的障害が半数以上の前駆期の被験者で認められた。全ての神経心理学的検査で統合失調症は前駆期被験者より有意な機能低下が認められた。対照より前駆期被験者で機能低下が認められた検査は、注意、言語性記憶の自由想起、言語流暢性試験、視覚記憶だった。

(抄訳者氏名：糸川昌成)

## エジンバラ・ハイリスク研究における転帰良好者と不良者の特徴の識別

Johnstone EC et al: Distinguishing characteristics of subjects with good and poor early outcome in the Edinburgh High-Risk Study. Br J Psychiatry Suppl 43: s26-29, 2002.

### 対象

エジンバラ・ハイリスク研究で対象となった被験者。2名以上近親者に統合失調症をもつ16歳から25歳の162名、年齢性別の一致した遺伝負因を持たない34名、年齢性別の一致した初発の統合失調症36例。

### 方法

18ヶ月ごとにPSE (present state examination)、脳のMRI撮影、神経心理学的検査を発症するか30歳になるまで続けた。voxel-based morphometry (VBM)を用いて精神病発病前後におけるMRI体積の個人内比較を行った。PSEのカテゴリーS+において、該当項目がなくどの時点でもスコアが0であった対象を転帰良好者(N=23, 男性12名、女性11名)と定義し、統合失調症を顕在発症した被験者(N=10, 男性7名、女性3名)と比較検討した。

### 結果と考察

神経心理学的検査ではWAIS-Rの動作性IQと言語性IQの差、計算、絵画完成、RBMT (Rivermead behavioural memory test)の標準化と物語、RAVLT (Rey auditory verbal learning test)の全体想起と遅延想起、SCOLP (speed and capacity of language processing)の単語同定で、転帰良好群が顕在発症群より有意に良好な成績を示した。MRIでは全脳容積が転帰良好群で有意に大きかった。女性では左右の視床核が有意に転帰良好群で大きかった。2回の撮影では有意ではないものの顕在発症群で両側の側頭葉が小さくなっていた。側頭葉の機能障害と容積減少が転帰不良の特徴である可能性が示唆された。

(抄訳者氏名：糸川昌成)

ニューヨーク・ハイリスク研究における統合失調症の親から生まれた子供の WCST の成績不良

Wolf LE et al: Wisconsin Card Sorting deficits in the offspring of schizophrenics in the New York High-Risk Project. Schizophr Res 57: 173, 2002.

#### 対象

ニューヨーク・ハイリスク研究 (NYHRP: New York high-risk project) で対象となった統合失調症の親を持つ子供 73 名 (年齢  $25.64 \pm 3.57$  歳、男性 59.51%)、気分障害の親を持つ子供 61 例 (年齢  $25.77 \pm 3.33$  歳、男性 39.61%)、健全な両親を持つ子供 120 名 (年齢  $25.42 \pm 3.09$  歳、男性 56.44%)。

#### 方法

WCST (Wisconsin card sorting test) を行いハイリスクの子供とリスクのない子供を比較検討した。

#### 結果と考察

課題の遂行維持、カテゴリーの完成が有意に統合失調症のハイリスク群で対照より悪かった。総誤反応数、保続誤反応数、保続応答数は対照と気分障害のハイリスク群のどちらと比較しても有意に統合失調症ハイリスク群で悪い成績だった。また、これら全ての項目で、顕在発症したハイリスク群 (N=13) の統合失調症は発症しなかったハイリスク群 (N=60) より有意に悪い成績だった。WCST の成績不良は発症脆弱性の指標にはなるが、ハイリスク対象の発症を予測することは出来ない。

(抄訳者氏名：糸川昌成)

統合失調症ハイリスクの若年者にみられる神経心理学的変化：エジンバラ・ハイリスク研究における神経心理学的評価の結果

Cosway R et al: Neuropsychological change in young people at high risk for schizophrenia: results from the first two neuropsychological assessments of the Edinburgh High Risk Study. Psychol Med 30: 1111-1121, 2000.

#### 対象

エジンバラ・ハイリスク研究に参加した統合失調症の親を持つ子供 78 例と年齢性別の一致した健康な両親を持つ子供 22 例。

#### 方法

18 ヶ月の間隔をおいて 2 回神経心理学的検査を行いハイリスク群と対照群を比較検討した。

#### 結果と考察

WAIS と NART の総得点のベースライン、WAIS-R の積み木と数唱の置き換え、RBMT (Rivermead Behavioural Memory Test)の物語の即時想起と遅延想起、言語流暢性試験、Hayling 文章完成試験のタイプB誤反応スコアでハイリスク群 (N=78) は対照群 (N=22) より有意に成績が悪かった。精神医学的評価の PSE (present state examination)のカテゴリ一S+におけるスコアが0か1の群 (N=59) と2か3の群 (N=19) を比較すると、スコアの高い群で有意に WAIS の総 IQ が低く、RBMT の物語の即時想起が悪かった。1 回目より 2 回目で PSE のスコアが増加した群 (N=5) と変化なかった群 (N=54) の比較では、WAIS と NART の総得点、WAIS-R の順行性数唱でスコア増加群で有意に成績が悪かった。

(抄訳者氏名：糸川昌成)

統合失調症関連精神病の予測因子としての小児期の注意、記憶、運動技能：ニューヨーク・ハイリスク研究

Erlenmeyer-Kimling L et al: Attention, memory, and motor skills as childhood predictors of schizophrenia-related psychoses: the New York High-Risk Project. Am J Psychiatry 157: 1416-1422, 2000.

#### 対象

ニューヨーク・ハイリスク研究（NYHRP: New York high-risk project）で対象となった 324 名のうち、小児期の神経心理学的検査結果がたどれた 269 名（統合失調症の親を持つ子供 79 名、気分障害の親を持つ子供 57 名、健康な両親を持つ子供 133 名）。

#### 方法

CPT (continuous performance test), ASP (attention span task), WISC (Wechsler intelligence scale for children)を用いて神経心理学的検査を行い、Lincoln-Oseretsky 運動発達スケールを用いて運動技能を評価した。

#### 結果と考察

統合失調症の親を持つ子供 79 名のうち 12 例が統合失調症関連精神病を発症し、28 名が気分障害を 13 例が他の I 軸の障害を発症した。言語性記憶、運動技能、注意に障害があった子供は、それぞれ 83%、75%、58%が統合失調症関連精神病を発症した。発症した被験者のうち 50%は 3 つとも障害が小児期に認められた。注意と記憶の疑陽性は、それぞれ 18%、28%だった。

（抄訳者氏名：糸川昌成）

精神病への移行に関与する HPAaxis 作用について : DEX/CRH 検査による検討

Thompson KN, Berger G, Phillips LJ et al. HPA axis functioning associated with transition to psychosis: combined DEX/CRH test. J Psychiatr Res 41: 446-450, 2007.

#### 対象

オーストラリア・メルボルン地区の PACE クリニック。精神病のウルトラハイリスク群 12 名の若年者 (平均年齢  $19.4 \pm 3.6$ , 15-25 歳、男 10/女性 2)。

#### 方法

デキサメサゾン副腎皮質刺激ホルモン放出ホルモン (DEX/CRH) 試験を用いて視床下部-下垂体-副腎系 (HPAaxis) の機能変化を検討した。BRPS, SANS, HAM うつ病スケール, HAM 不安スケール, GAF, LEIS ライフイベント尺度, Hassles Scale。

#### 結果と考察

2 年間で 12 名のうちの 3 人について急性精神病状態を呈した。精神病への非移行群の方が精神病移行群に比較して高いコルチゾールレベルであった。抑うつ尺度と不安症状の重症度と同様であった。これらの予備的結果は、精神病のハイリスク群における HPAaxis の機能異常が精神病発症の過程よりうつ病の併発に関与する可能性があることを示している。

(抄訳者氏名 : 谷井久志)

## ハイリスク群におけるストレスと HPA 系の検討

Thompson KN, Philips LJ, Komesaroff P et al. Stress and HPA-axis functioning in young people at ultra high risk for psychosis. J Psychiatr Res 41: 561-569, 2007.

### 対象

オーストラリア・メルボルン地区の PACE クリニック。UHR 基準を満たした 23 人の若年者（平均年齢  $18.9 \pm 3.3$ , 15-25 歳、男 14/女性 9）。

### 方法

血漿サンプルによるコルチゾールと糖質コルチコイドレセプター数の測定、BRPS, SANS, HAM うつ病スケール, HAM 不安スケール, QLS, GAF, LEIS ライフイベント尺度, Hassles Scale、MRI スキャンが行われた。

### 結果と考察

血漿コルチゾール濃度は、ストレスを伴う出来事の体験ではなく『気苦労』の経験を有意な相関があった。抑うつ不安症状と血漿コルチゾール濃度についても有意な相関が見いだされた。血漿コルチゾール濃度と精神病理所見、精神症候学、神経の機能障害、下垂体・海馬体積の間には有意な関連は見いだされなかった。

視床下部-下垂体-副腎（HPA）系機能障害がストレス負荷と精神病症状発現に関与することが想定され、本研究はウルトラハイリスク（UHR）群における精神病症状の発現において HPA 系の関与を検証することを目的としている。UHR が経験する Hassles がコルチゾール濃度を上昇させることを示唆する。更にうつ病患者と不安症状の重症度に影響を及ぼす可能性がある。血漿コルチゾール濃度と精神病症状、海馬および下垂体体積の間には相関は認められなかった。精神病症状の発現初期に HPA 系機能障害の可能性はあるが、更なる検討が必要である。

（抄訳者氏名：谷井久志）

## 精神病前駆期を対象とするオランザピン・プラセボの無作為二重盲検試験

McGlashan TH et al: Randomized double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. Am J Psychiatry 163: 790-799, 2006.

### 対象

Prevention Through Risk Identification, Management と Education プロジェクトとして北米の4医療機関（エール大学、トロント、ノースカロライナ、カルガリ）で行われた。

### 方法

外来患者を対象に1年間の二重盲検治療期間においてオランザピン（5-15mg/日、N=31）またはプラセボ（N=29）を投与され、その後の1年間の未治療期間（追跡期間）が設定された。有効性の判定は精神病への移行率を含む Prodromal Symptoms Scale をスコア化した。評価内容は PANSS, CGI, MADRS, YMRS, GAF などであった。

### 結果と考察

治療期間内でオランザピン治療患者の 16.1%、プラセボ治療患者の 37.9%が精神病への移行を示した。プラセボ患者の間の移行のリスクはオランザピン治療患者の約 2.5 倍でありほぼ有意な差が認められた。その後の継続期間における移行率は、群間で有意差がなかった。治療期間内で前駆期の陽性症状の平均スコアはオランザピン群がプラセボ群よりも改善効果を示した。オランザピンにおいて第 8 週と第 28 週の間で有意な改善効果が認められた。しかしオランザピンによる治療を受けた患者では有意な体重増加があった（オランザピン群で 8.79 kg±9.05kg vs 対照群で 0.30 kg±4.24kg）。

統合失調症の前駆症状発現時期における精神病への移行を遅延・予防し、発症を減少させる上でのオランザピンの効果を検討した。治療の違いによる精神病への移行率については有意な相違は認められなかったが、低い検出力も影響しており、ほぼ有意な差異としてオランザピンが移行率を低下させること、精神病の発症を遅延する可能性を示唆している。オランザピンは前駆的な陽性症状に対する改善効果があったが、体重増加を誘発した。本研究では精神病前駆期における治療的介入研究の重要性を示している。

（抄訳者氏名：谷井久志）



閾値下の臨床症状を有する群において精神病発症リスクを軽減させることを目的とした治療的介入に関する RCT

McGorry PD et al: Randomized controlled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with subthreshold symptoms. Arch Gen Psychiatry 59: 921-928, 2002.

#### 対象

オーストラリア・メルボルン地区の PACE クリニック。精神病ウルトラハイリスク群の 59 人（平均年齢  $20\pm 3.6$ , 14-28 歳、男 34/女性 25）。

#### 方法

介入群（Needs-based 介入）については低用量リスペリドン療法（平均投薬量、1.3mg/d）と認知行動療法治療群とを比較された。治療期間は 6 ヶ月間であった。治療期間後も全患者に対し治療が継続された。臨床評価は治療開始時（ベースライン）、開始後 6 ヶ月と 12 ヶ月に行われた。評価内容は BRPS, SANS, HAM うつ病スケール, HAM 不安スケール, QLS, YMS, GAF, MRI スキャン

#### 結果と考察

治療的介入がなされた 28 人中 10 人は治療終了までに精神病の発症があり、特定の予防的介入群は 31 人中 3 であった ( $P=.03$ )。6 ヶ月の追跡調査の後、特定の予防的介入群のさらに 3 人は精神病に移行した。この時点での intention-to-treat 解析ではその差は有意ではなかった ( $P=.24$ )。しかし特定の予防的介入群のリスペリドン治療患者に対する進行予防効果はリスペリドン使用中止後でも 6 ヶ月間の効果があった。

精神病性疾患（特に統合失調症）による障害は発症初期に生じるためこの期間内における介入の必要性は理解されているが、この時期の治療介入の試みはごく最近である。特別の薬物療法と精神療法はハイリスク群における早期精神病の発症リスクを下げ、発症を遅らせる効果（有病率減少）と発生率の若干の減少を意味する。

（抄訳者氏名：谷井久志）

# Ⅲ. 研究成果の刊行 に関する一覧

## 平成19年度 研究成果の刊行に関する一覧表 (課題番号:H19-こころ-一般-012)

## 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
該当なし							

## 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
Nishida A, Tanii H, Nishimura Y, Kaji ki N, Inoue K, Okada M, Sasaki T, Okazaki Y	Associations between psychotic-like experiences and mental health status and other psychopathology among Japanese early teens	Schizophrenia Research,	99・1	125-133	2008
西田淳志、針間博彦、石倉習子	英国の精神保健スタンダード&マニュアル(抜粋紹介)	こころの科学	133	72-78	2007
岡崎祐士	早期治療とは何か	こころの科学	133	8-12	2007
西田淳志	早期精神障害への支援と治療—その根拠と目的	こころの科学	133	13-19	2007
小林啓之・水野雅文	早期診断・治療の実際	こころの科学	133	20-26	2007
茅野 分・水野雅文	メルボルンにおける早期介入サービスの実例—ORYGENユースヘルス	こころの科学	133	26-32	2007
生野照子	摂食障害の早期治療と自助組織	こころの科学	133	45-49	2007
伊藤弘人	医療費適正化と精神障害予防	こころの科学	133	67-71	2007
岡崎祐士	早期精神障害とは何か	臨床精神医学	36(4)	353-357	2007
小林啓之・水野雅文	早期診断と治療の根拠	臨床精神医学	36(4)	377-382	2007
西田淳志	早期精神障害における思春期精神病様体験(PLEs)	臨床精神医学	36(4)	383-389	2007
笠井清登	統合失調症脳画像研究と早期診断	臨床精神医学	36(4)	405-408	2007
野中 猛	早期治療介入を軸とする精神科医療システムの改革	臨床精神医学	36(4)	409-414	2007

針間博彦、石倉習子、西田淳志、徳永太郎、石川陽一、内海香里、大澤有香、神納光平、大倉雅、石本佳代、江尻真樹、今井淳司、浅野未苗、岡崎祐士	英国における早期治療介入の医療制度化の経緯と実際、	臨床精神医学	36(4)	391-402	2007
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# IV. 研究成果の刊 行物・別刷一覧



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Schizophrenia Research xx (2007) xxx–xxx

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## Associations between psychotic-like experiences and mental health status and other psychopathologies among Japanese early teens

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Received 1 September 2007; received in revised form 18 November 2007; accepted 30 November 2007

### 1. Introduction

Psychotic-like experiences (PLEs) occur not only in persons with psychotic disorders, but also in the general population (van Os, 2003; Kendler et al., 1996). Some longitudinal studies have reported that PLEs in childhood and adolescence may be risk factors for later psychiatric disorders and poor psychosocial outcome. A recent birth cohort study in New Zealand indicated that self-reported PLEs at age 11 years were highly predictive of a diagnosis of schizophreniform disorder at age 26 (Poulton et al., 2000). Other longitudinal studies reported that PLEs in adolescents and adults tended to predict future mental disorders, such as depression and substance use disorders (Chapman et al., 1994; Dhossche et al., 2002; Hanssen et al., 2005; Verdoux et al., 1999).

Thus far, however, little is known about the mental health status of children and adolescents with PLEs in a general population sample. Few studies have explored the psychosocial factors and psychopathological difficulties associated with PLEs in young people (Poulton et al., 2000; Lataster et al., 2006) at a crucial age for the precipitation or prevention of mental disorders. If we

can identify children and adolescents with PLEs and provide support for them from the early developmental stages, we may be able to prevent the further development of mental disorders later in life.

The aim of this study was to investigate the prevalence of PLEs and the relationships between the severity of PLEs and the prevalence of poor mental health status in Japanese early teens. Psychopathological factors, victimization, lifestyle, and help-seeking actions that may be associated with PLEs were also explored. A school-based cross-sectional survey was conducted.

### 2. Methods

#### 2.1. Sample and survey procedures

In July 2006, we conducted a school-based cross-sectional survey of the psychopathologies and lifestyles of early teens in the city of Tsu, Mie Prefecture, Japan (ESPAT: Epidemiological Study of Psychopathology of Adolescents in Tsu). Mie Prefecture is in the center of Japan, and Tsu (population 280,000) is the prefectural capital. Tsu's rates of unemployment and suicide are almost equal to Japan's national averages (Bureau of Statistics, Ministry of Internal Affairs and Communications of Japan, 2007).

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The self-reported questionnaire targeted junior high school students (7th to 9th grade, ages 12–15 years); this level of schooling is compulsory in Japan. There are 20 public junior high schools in Tsu, with 7127 students in total. After the study plan was approved by the ethics committee of Mie University School of Medicine, the principal investigators (A.N. & Y.O.) requested the school principals' cooperation with the study. After consulting with teachers and parents, 14 of the 20 principals agreed to the proposal.

Classroom instructors were trained to follow guidelines for the distribution and collection of the questionnaires. The instructors distributed a questionnaire and envelope to each student and explained these guidelines to the class: (1) participation was anonymous and voluntary, and (2) answers to the questionnaire absolutely would not be seen by the teachers. The students were instructed to seal the questionnaire in the envelope immediately after completing it. Each instructor also reported the number of attending and absent students (including those who had not attended for more than 1 month) on the day of the survey. Research staff collected the sealed questionnaires immediately after completion at each school.

## 2.2. Measures

The questionnaire consisted of items regarding (a) psychopathological and behavioral problems including PLEs, (b) mental health status as measured by the Japanese version of the 12-item General Health Questionnaire (GHQ-12), and (c) other variables, including lifestyle, victimization, interpersonal and help-seeking attitudes, and demographic characteristics. One psychologist (N. K.) who is an expert in child and adolescent psychology and three schoolteachers at public junior high schools in Tsu (including one teacher of the Japanese language) were involved in designing the questions; they determined whether or not public junior high school students in Tsu would be able to understand them.

### 2.2.1. Psychopathological and behavioral problems

**2.2.1.1. PLEs.** PLEs were assessed using four items adopted from the schizophrenia section of the Diagnostic Interview Schedule for Children (DISC-C) (Costello et al., 1982). These items were previously used in a birth cohort study and were good predictors of schizophreniform disorder in adulthood (Poulton et al., 2000). The items were as follows: (I) "Some people believe in mind reading or being psychic. Have other

people ever read your mind?"; (II) "Have you ever had messages sent just to you through the television or radio?"; (III) "Have you ever thought that people are following you or spying on you?"; and (IV) "Have you ever heard voices other people cannot hear?" All responses were made on a three-point scale: 'no', 'yes, likely', and 'yes, definitely'. We defined 'no' as no experience, 'yes, likely' as a probable experience, and 'yes, definitely' as a definite experience for each hallucinatory and delusional experience. A score of '1' was allotted to both probable and definite experience, and '0' to no experience. Scores of '1' were added together to form the total PLE score, with a range of 0 to 4. The presence of PLEs was defined as a total PLE score  $\geq 1$ .

**2.2.1.2. Other psychopathologies and behavioral problems.** In addition to PLEs, the questionnaire asked about the following psychopathological and behavioral problems: (i) strong anxiety in class (within 1 month), (ii) suicidal ideation (ever), (iii) self-harming behaviors (within 1 year), (iv) physically assaulting others (within 1 year), (v) bullying others (within 1 year), (vi) irritability when exchanging e-mails (within 1 week), (vii) self-induced vomiting for the purpose of dieting (ever), (viii) difficulty falling asleep due to hypersensitivity to noises (within 1 month), and (ix) difficulty concentrating due to hypersensitivity to noises (within 1 month). These items, except (vi), were based on some previous findings on the symptoms and pre-morbid characteristics of psychosis and related conditions (Jones et al., 1994; Kim-Cohen et al., 2003; Inskip et al., 1998; Haw et al., 2005; Done et al., 1994; Arseneault et al., 2003; Cannon et al., 2001; McGhie and Chapman, 1961; Bunney et al., 1999). See Appendix for details.

Items (i), (ii), (vi), (viii), and (ix) were rated using a four-point scale, while items (iii), (iv), (v), and (vii) were rated as "yes" or "no".

### 2.2.2. Mental health status

**2.2.2.1. The General Health Questionnaire (GHQ-12).** The 12-item General Health Questionnaire (GHQ-12) is one of the most widely used self-report screening tools for non-psychotic mental illnesses, particularly symptoms of anxiety or depression (Goldberg et al., 1976). The validity and reliability of the Japanese version of the GHQ-12 has been confirmed (Fukunishi, 1990; Doi and Minowa, 2003). The GHQ was originally applied to adult populations and subsequently used and validated for younger populations

Table 1  
Demographic variables and mean General Health Questionnaire (GHQ-12) scores by school grade ( $N=4894$ : male, 2523; female, 2371)

School grade	<i>N</i>	Age Mean	Family structure						GHQ-12 score		Prevalence of GHQ-12 score $\geq 4$	
			With both parents		With one parent		Apart from parents		Mean	SD	<i>N</i>	%
Grade 7	1580	12.30	1357	85.89	192	12.15	31	1.96	2.72	2.61	516	32.66
Grade 8	1645	13.29	1381	83.95	234	14.22	30	1.82	3.15	2.79	646	39.27
Grade 9	1669	14.31	1374	82.32	256	15.34	39	2.34	3.70	2.93	785	47.03
Overall	4894	13.32	4112	84.02	682	13.94	100	2.04	3.20	2.81	1947	39.78

(Radovanovic and Eric, 1983; D'Arcy and Siddique, 1984; Arakida et al., 2003; Kaneita et al., 2007).

A four-point scale with binary scoring (0011), known as the GHQ method, was used to answer each question. Answers of '1' were then added together to form the total score, with a range of 0 (best possible) to 12 (worst possible). Subjects with a total GHQ-12 score  $\geq 4$  were considered to have poor mental health, according to previous studies (Arakida et al., 2003; Fuchino et al., 2003; Kaneita et al., 2007).

### 2.2.3. Other variables

The questions related to lifestyle covered (i) drinking alcohol (within 1 month), (ii) smoking (within 1 month), (iii) use of recreational drugs (ever), and (iv) hours of watching TV and/or using personal computers (per day, currently). See Appendix for details.

Items (i), (ii), and (iii) were rated "once or more" or "not at all". Item (iv) was rated using a five-point scale.

The questions related to victimization included (i) being bullied (within 1 year) and (ii) violence from adults in the home (within 1 month). Both items were answered with either "yes" or "no".

Three questions concerned interpersonal and help-seeking attitudes: (i) preference for being alone or with

others, (ii) number of people one can consult (5-point scale), (iii) current contact with medical services ("yes" or "no"). See Appendix for details.

The questionnaire also included items about demographic variables including sex, school grade, and family structure, i.e., living apart from parents, living with one parent, or living with both parents.

### 2.3. Statistical analysis

The relationships between the severity of PLEs and the prevalence of poor mental health status by GHQ-12 were assessed by dividing the PLEs into three groups (a 'no PLE group' defined by a total score of 0; a '1 PLE group' defined by a total score of 1; and a '2 or more PLEs group' defined by a total score of  $\geq 2$ ) (Lataster et al., 2006). The Cochran–Armitage trend test and logistic regression analysis adjusted for age and sex were used for the statistical analysis.

We investigated the factors associated with the presence of PLEs (experiencing at least one PLE) by using logistic regression analysis. First, variables except for the GHQ-12 score were entered individually to obtain unadjusted odds ratios. Second, the variables were entered together in a stepwise logistic regression model

Table 2  
Associations between the severity of psychotic-like experiences (PLEs) and poor mental health status in Japanese early teens ( $N=4894$ )

Psychotic-like experiences (PLEs) <sup>a)</sup>	Prevalence of poor mental health (GHQ-12 <sup>b)</sup> score $\geq 4$ )		OR	Odds ratio <sup>c)</sup> 95% CI	<i>p</i> -value <sup>d)</sup>
	<i>N</i>	%			
No symptom group ( $N=3089$ )	942	30.5	1.00		<0.001
1 symptom group ( $N=1063$ )	526	49.5	2.19	1.89–253	
2 or more symptoms group ( $N=742$ )	479	64.5	4.14	3.48–4.93	

<sup>a)</sup> No symptom group= Individuals with no probable and/or definite PLE.

1 symptom group= Individuals with one probable or definite PLE.

2 or more symptoms group= Individuals with two or more probable and/or definite PLEs.

<sup>b)</sup> GHQ-12: 12-item General Health Questionnaire.

<sup>c)</sup> Odds ratios adjusted for age and sex.

<sup>d)</sup> *P*-value of logistic regression analysis adjusted for age and sex.



to obtain the odds ratios adjusted for the interrelationships between these variables.

When the answers to all items with a four-point scale were used as covariates in multivariate logistic regression analysis, they were converted into binary scoring (0011).

All statistical analyses were carried out using SPSS (Statistical Package for Social Sciences) version 15.0 for Windows. A  $p$ -value  $< 0.05$  was considered statistically significant.

### 3. Results

#### 3.1. Descriptive statistics

Fourteen of the 20 public junior high schools in Tsu cooperated with this survey. Of a total of 5335 students in the 14 schools, 205 students (3.8%) were absent (57 of whom had been absent for at least a month) on the day of the survey. Among the rest, 18 (0.3%) did not agree to

Table 3  
Factors associated with psychotic-like experiences (PLEs) in Japanese early teens ( $n=4561$ ), analyzed with logistic regression<sup>a) b)</sup>

Variable	Parameter	Unadjusted odds ratios			Adjusted odds ratios <sup>c)</sup>		
		OR	95% CI	$p$ value	OR	95% CI	$p$ value
<i>Demographic characteristics</i>							
Sex	female / male	1.37	1.22–1.53	<0.001			
School grade					n. s.		
7							
8	8/7	1.06	0.92–1.22				
9	9/7	1.10	0.95–1.27				
Family structure					n. s.		
Apart from parents							
With one parent	with one parent / apart from parents	0.69	0.45–1.05				
With both parents	with both parents / apart from parents	0.65	0.44–0.96				
<i>Psychopathologies</i>							
Strong anxiety in class	often, always / never, rarely	2.05	1.78–2.36	<0.001	1.39	1.19–1.63	<0.001
Suicidal ideation	possibly, yes / no, probably not	2.98	2.64–3.37	<0.001	2.10	1.83–2.41	<0.001
Self-harming behaviors	yes / no	3.49	2.67–4.57	<0.001	1.37	1.00–1.86	0.047
Physically assaulting others	yes / no	1.80	1.52–2.12	<0.001	1.26	1.04–1.52	0.020
Bullying others	yes / no	1.81	1.58–2.07	<0.001	1.30	1.11–1.53	0.001
Irritability when exchanging e-mails	twice, three times or more / never, once	2.40	1.96–2.94	<0.001	1.30	1.03–1.64	0.030
Self-induced vomiting for the purpose of dieting	yes / no	2.67	1.65–4.31	<0.001			
Difficulty falling asleep due to hypersensitivity to noises	often, always / never, rarely	2.58	2.18–3.05	<0.001	1.66	1.38–2.01	<0.001
Difficulty concentrating due to hypersensitivity to noises	often, always / never, rarely	2.18	1.92–2.47	<0.001	1.53	1.32–1.76	<0.001
<i>Other variables</i>							
Alcohol	once or more / not at all	2.18	1.82–2.61	<0.001	1.71	1.39–2.09	<0.001
Smoking	once or more / not at all	3.44	2.14–5.53	<0.001			
Recreational drugs	once or more / not at all	2.61	1.61–4.22	<0.001	1.96	1.15–3.36	0.014
Length / day of watching T V and / or using PC (h)					<0.001		
0							
≤1	≤1 / 0	0.81	0.69–0.94				
1<, ≤2	1<, ≤2 / 0	0.97	0.82–1.15				
2<, ≤3	2<, ≤3 / 0	0.94	0.77–1.16				
3<	3< / 0	1.49	1.20–1.84				
Violence from adults in the home	yes / no	2.93	2.31–3.72	<0.001	1.74	1.32–2.29	<0.001
Being bullied	yes / no	2.43	2.09–2.81	<0.001	1.59	1.34–1.89	<0.001
Being alone or with others	with others / alone	0.68	0.60–0.77	<0.001			
Number of people one can confide in	three, four or more / none, one, two	0.82	0.73–0.92	0.001			
Current contact with medical services	yes / no	1.72	1.49–1.98	<0.001	1.45	1.23–1.70	<0.001

<sup>a)</sup> Students with psychotic-like experiences, 1; Students without psychotic-like experiences, 0.

<sup>b)</sup> In each section, the missing data have been excluded from the statistical analyses.

<sup>c)</sup> Stepwise logistic regression model.

participate in the survey. Altogether, 5073 students (95.1% of the students in the participating schools) returned sealed questionnaires, but 179 students gave incomplete responses on crucial items (PLEs, sex, school grade, family structure, GHQ-12). We were finally able to analyze the responses of 4894 students (mean age, 13.3 years  $\pm$  0.9), including 2523 boys (51.6%) and 2371 girls (48.4%), representing 68.7% of all public junior high school students in Tsu (Table 1).

The GHQ-12 showed good internal consistency. The Cronbach  $\alpha$  of GHQ-12 for the whole sample was 0.80. Mean GHQ-12 scores and the prevalence of poor mental health (GHQ-12 scores  $\geq$  4) were higher at the higher grades (Table 1).

### 3.2. Prevalence of PLEs and the association with poor mental health status

The number of subjects reporting at least one definite PLE was 746 (15.2%) (357 boys, 389 girls). The number of subjects reporting at least one probable and/or definite PLE was 1805 (36.9%) (842 boys, 963 girls). As summarized in Table 2, the severity of PLEs was significantly related to poor mental health status after controlling the effects of age and sex.

### 3.3. Associations between PLEs and psychopathologies and other variables

The results of univariate and multivariate logistic regression analyses of the association between PLEs and the other variables are shown in Table 3. Univariate analyses showed significant associations between PLEs and most of the variables; the exceptions were school grade and family structure. Multivariate analyses showed significant associations between PLEs and strong anxiety in class, suicidal ideations, self-harming behaviors, physically assaulting others, bullying others, irritability when exchanging e-mails, difficulty falling asleep due to hypersensitivity to noises, difficulty concentrating due to hypersensitivity to noises, drinking alcohol, using recreational drugs, being the subject of violence from adults at home, being bullied, and current contact with medical services.

## 4. Discussion

### 4.1. Mental health status in this sample

The mean GHQ-12 score for the total sample was  $3.2 \pm 2.8$ . This was similar to the results of previous studies of junior high school students in Japan (Arakida et al.,

2003; Kaneita et al., 2007), which found mean GHQ-12 scores of 3.2–3.3. The prevalence of poor mental health status defined by GHQ-12 score  $\geq$  4 in our overall sample was 39.8%. This strikingly high prevalence was consistent with another recent nationwide cross-sectional study of 38,090 junior high school students in Japan, which observed a prevalence of 38.3% (Kaneita et al., 2007).

### 4.2. Prevalence of PLEs

A number of studies have reported on the prevalence of PLEs in adult community populations (reviewed by van Os, 2003), while only a few studies have targeted early teens (Poulton et al., 2000; Lataster et al., 2006). To the best of our knowledge, our current study has the largest sample among those investigating PLE prevalence in an early teen community population.

The prevalence of PLEs in Japanese early teens was comparable with that in early teens in New Zealand or the Netherlands. In this study, we adopted PLE items that had already been used in a birth cohort study in New Zealand (Poulton et al., 2000). In that longitudinal study, a structured interview using the items was conducted for children aged 11 ( $n=761$ ), of whom 14.7% reported PLEs. In our study, early teens aged 12–15 years were asked to answer the same items using self-reported questionnaires, and 15.2% reported a definite experience of at least one PLE item. A similar result was also found in a school-based health survey in the Netherlands ( $n=1290$ ) using the same PLE items on a questionnaire (mean age, 14 years; 19.1% reported PLEs) (Lataster et al., 2006).

### 4.3. Mental health status and psychopathological characteristics of early teens with PLEs

Previous studies observed associations between PLEs and psychopathologies such as neurotic symptoms, substance dependence (Johns et al., 2004), and criminally violent behaviors (Mojtabai, 2006) in adult community populations. However, thus far, few studies have examined the association between PLEs and mental health status and psychopathologies in children and adolescents. The primary contribution of this study is in revealing the association between PLEs and poor mental health and other psychopathologies in a general population of early teens.

The present study revealed a significant association between the severity of PLEs and poor mental health status measured by GHQ-12, which mainly assessed symptoms of depression and anxiety. Associations were

also observed between PLEs and both strong anxiety in the classroom and suicidal ideation. Anxiety in social situations and suicidal ideation are respectively representative symptoms of anxiety and depression, respectively. Our results indicated that PLEs in early developmental stage were associated with anxiety and depression. This may be consistent with several previous studies, which observed associations between PLEs and anxiety or depression (Dhossche et al., 2002; Johns et al., 2004). Our observation could also be interpreted to suggest that PLEs are associated with other mental disorders, including schizophrenia and other psychoses. Anxiety and depression are common characteristics in the pre-morbid personality of schizophrenia (Davidson et al., 1999; Malmberg et al., 1998; Jones et al., 1994) or a prodromal symptom of psychoses (Hafner et al., 2005; Yung et al., 2007).

The teens with PLEs seemed to be more sensitive to environmental noises. Significant associations were observed between PLEs and difficulty falling asleep or concentrating due to hypersensitivity to environmental noise. Hypersensitivity to sensory stimuli, such as environmental noise, is one of the perceptual anomalies in schizophrenia (McGhie and Chapman, 1961; Bunney et al., 1999). However, this hypersensitivity to environmental noise, which may be associated with sensory gating deficits, may exist not only in schizophrenia but also in a large range of mental disorders, such as mania (Adler et al., 1990), depression (Vandoolaeghe et al., 1998), and anxiety disorders (Ludewig et al., 2002). Hence, PLEs in adolescents might be considered non-specific markers of poor mental health in several mental disorders, including anxiety disorders and mood disorders, not only in schizophrenia.

We also observed significant associations between PLEs and both physically assaulting others and bullying others. A birth cohort study in New Zealand reported that childhood psychotic symptoms were a strong risk factor for violence in adults with schizophreniform disorder (Arseneault et al., 2003). A large cross-sectional study in the U.S. also reported a significant association between PLEs and violent behaviors in an adult community population (Mojtabai, 2006). Our current results suggested that, in an earlier developmental stage, PLEs are associated with interpersonal problems, such as bullying or physically assaulting others.

A recent national survey revealed that 68.4 % of Japanese junior high school students owned their own cellular phones, of which 67.8% reported that they exchanged e-mails or text messages more than 10 times per day (National Police Agency of Japan, 2005). In Japan, an 11-year-old girl fatally stabbed a classmate in

their schoolyard after an intense online argument (Nakamura, 2004). After this incident, interpersonal problems (e.g., cyber-bullying) and psychopathology associated with the online communication among youth have gained increasing attention from education and mental health professionals in Japan. The reason for the association between PLEs and irritability when exchanging e-mails and text messages remains unclear; however, it is possible that adolescents with PLEs might be more vulnerable to stress in interpersonal online communication than those without PLEs.

PLEs were associated with self-harming behaviors among present Japanese youth. Self-harming behaviors at a young age may be an important indicator of mental health problems and a strong risk factor for subsequent suicidal behaviors in later life (Portzky and van Heeringen, 2007). Longitudinal observation might be of use for future prevention and early intervention of mental health problems and suicidal behaviors in the youths with PLEs.

#### 4.4. Associations of other variables

Among variables other than those of psychopathologies, significant associations with PLEs were observed for substance use (alcohol use, recreational drugs), victimization (being bullied, violence from adults in the home), and contact with medical services.

A previous study reported that adults with PLEs in a community sample were more likely to be alcohol- or cannabis-dependent than adults without PLEs (Johns et al., 2004). Our results indicated that PLEs in earlier developmental periods were also significantly associated with substance use.

In this study, PLEs in early teens were also associated with victimizing experiences such as violence from adults in the home and being bullied. This finding agreed with the result of a recent similar study in the Netherlands, which found an association between PLEs in early teens and the experience of being bullied, using the same PLE items as in our study (Lataster et al., 2006).

The present results also suggested that early teens with PLEs in a general population have more current contact with medical services due to some physical or mental distresses than those without PLEs. It might be speculated that general practitioners have a crucial role in identifying PLE-positive early teens with distress.

#### 4.5. Methodological considerations and future research

The present research sample of early teens was, as far as we know, the largest ever examined for this purpose, and the participation rate for this survey was high.

However, the results contain some limitations. First, as this was a school-based study, we could not obtain answers from absent students. Poor mental health status and psychopathology may be more prevalent among frequently or long-absent students. Therefore, the prevalence of psychopathology and poor mental status detected in this study is likely to be underestimated. Second, as this was a self-reported questionnaire, it might include more over-reporting and/or under-reporting on certain topics than an interview-based survey would. Third, as we used a cross-sectional survey, we could not conclude cause-and-effect relationships between PLEs and other factors. One follow-up study showed that hallucinatory experiences in childhood most frequently resolved within 3 years (Escher et al., 2002). Hence, in the future, a follow-up study will be needed to investigate the nature of the relationships between PLEs in early developmental periods and outcomes later in life.

#### Role of funding source

Funding for this study was provided by the Research Group for Schizophrenia in Japan. The Research Group for Schizophrenia in Japan had no further role in study design, in the collection, analysis and interpretation of data, in writing of the report, and in the decision to submit the paper for publication.

#### Contributors

Mr. Nishida and Dr. Okazaki designed the study and wrote the protocol. Dr. Sasaki and Dr. Nishimura undertook the statistical analysis, and Dr. Okazaki and Mr. Nishida interpreted the data. Mr. Nishida and Dr. Tani wrote the first draft of the manuscript and Dr. Inoue, Dr. Okada and Ms. Kajiki managed the literature searches and revised the first draft critically. All authors contributed to and have approved the final manuscript.

#### Conflict of interest

All authors declare that they have no conflict of interest.

#### Acknowledgements

The authors thank the Board of Education of Tsu-city for their cooperation and assistance in conducting this research. We are grateful also to other members of the research assistants, in particular Mr. Teppei Takami, Mr. Yu Kakimoto and Ms. Reina Hojo of Mie University, for their cooperation with the study.

This research was supported by a grant-in-aid from the Research Group for Schizophrenia in Japan (Mr. Atsushi Nishida). A.N. acknowledges support from the Research Group for Schizophrenia in Japan, Award for Research Excellence.

#### Appendix

The survey items on psychopathologies and other variables are outlined below. The items for psychotic-like experiences are described in the text.

Psychopathological and behavioral problems  
*Strong anxiety in the classroom*

- *Question:* How often in the past month have you had anxiety or uncontrollable nervousness when speaking in front of the class (i.e., stuttering, shaking hands, etc.)?
- *Answer:* (0) never, (1) rarely, (2) often, (3) always

#### *Suicidal ideation*

- *Question:* Have you ever had thoughts that your life is no longer worth living?
- *Answer:* (0) no, (1) probably not, (2) possibly, (3) yes

#### *Self-harming behaviors*

- *Question:* Have you intentionally hurt yourself within the past year?
- *Answer:* (0) no, (1) yes

#### *Physically assaulting others*

- *Question:* Have you physically assaulted another person within the past year?
- *Answer:* (0) no, (1) yes

#### *Bullying others*

- *Question:* Have you bullied another person within the past year?
- *Answer:* (0) no, (1) yes

#### *Irritability when exchanging e-mails*

- *Question:* How often in that past week have you suffered from irritation when exchanging e-mails or text messages with others?
- *Answer:* (0) never, (1) once, (2) twice, (3) three times or more

#### *Self-induced vomiting for the purpose of dieting*

- *Question:* Have you ever intentionally vomited (thrown up) after eating in order to lose weight?
- *Answer:* (0) no, (1) yes

#### *Difficulty falling asleep due to hypersensitivity to environmental noises*

- *Question:* How often in the past month have you had difficulty falling asleep because of environmental noises that bothered you?
- *Answer:* (0) never, (1) rarely, (2) often, (3) always