

統合失調症治療の最前線

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1 はじめに

クロルプロマジンの発見以来、統合失調症の治療の主役を薬物療法が演じてきた。しかしながら従来の薬物療法では、効果が乏しい症状や副作用としての障害を残す例も多く見られ、薬物療法を多様な治療技法の1つと位置付けた包括的な治療の実践が求められつつある。最近では、初回エピソード統合失調症における治療こそ長期予後の改善のために重要であることが強く意識され、薬効を最大限に生かすためには、早期発見、早期治療や、発症後3~5年といわれる治療臨界期における集中的治療などが重要であることが認識されてきている。また、服薬アドヒアランスの改善や、飲みやすい非定型抗精神病薬剤の開発も図られている。一方で、新たに代謝系副作用などの課題も見つかってきている。さらに後述するように、最新の研究結果¹⁾によれば、抗精神病薬の使用自体が脳体積の進行性の萎縮に関与している可能性も示唆されており、抗精神病薬の使用量を必要最低限に抑える重要性がより強調されつつある。

本稿ではこれらの問題点を整理しながら、これからの統合失調症治療における薬物療法への期待とあり方を探っていく。

2 非定型抗精神病薬と定型抗精神病薬の比較

非定型抗精神病薬は、第2世代抗精神病薬とも呼ばれ、幾つかのタイプが存在する。ドパミンD₂受容体アンタゴニスト作用に加えセロトニン受容体アンタゴニスト作用も有するserotonin-dopamine antagonist (SDA)は、より錐体外路症状の発現を抑

える。また、幅広い受容体結合能のスペクトラムと比較的緩やかなドパミンD₂受容体遮断作用を有するmulti-acting receptor-targeted antipsychotics (MARTA)や、ドパミン部分アゴニスト(partial agonist)作用を有する非定型抗精神病薬も開発され、統合失調症の薬物療法の選択肢が広がってきた。非定型抗精神病薬の登場で、それまでの抗精神病薬は定型もしくは第1世代抗精神病薬などと呼ばれるようになり、非定型抗精神病薬の卓越性が強調されてきたが、近年ではその卓越性に対する否定的な見解も出現してきており、加えて非定型抗精神病薬の新たな課題も報告されるようになってきている。

非定型抗精神病薬が登場した当初の研究結果では、定型抗精神病薬に比べて非定型抗精神病薬の方が錐体外路症状のリスクが少ないだけでなく、統合失調症の陽性症状や陰性症状に対してもより有効であると報告されてきた。しかし、その多くの研究デザインは定型抗精神病薬として中等量から高用量のハロペリドールを使用した比較研究であった。²⁾ ハロペリドールは定型抗精神病薬を代表する薬の1つではあるが、中等量から高用量使用した場合、錐体外路症状が出現しやすく、そのために継続困難となったり、精神症状と判別が困難なアカシジアや運動減退が出現する可能性がある。実際、後年、定型抗精神病薬の用量を錐体外路症状の出現を最小限にするように抑えた研究では、非定型抗精神病薬と定型抗精神病薬の間に有効性については差がないことが示唆されている。2005年に発表されたCATIE (Clinical Antipsychotic Trials of Intervention Effectiveness)³⁾では、定型抗精神病薬としてペルフェナジンが使用され、2006年に発表されたCUtLASS (Cost Utility of the Latest Antipsychotic Drug in Schizophrenia Study)⁴⁾では、定型抗精神病

薬群の約半数にスルピリドが使用されたが、いずれの研究においても定型抗精神病薬に対する非定型抗精神病薬の優位性は証明されなかった。

また錐体外路症状は、非定型抗精神病薬において全く出現しないわけではない。PET を使用し、非定型抗精神病薬のリスペリドンによる脳内のドパミンレセプターの占有率と錐体外路症状の関係性を調べた研究では、脳内ドパミン D_2 受容体の占有率が約 70% 以上で抗精神病作用を発揮するが、占有率が 80% 以上になると錐体外路症状が出現しやすいことが報告された。⁵⁾

非定型抗精神病薬は定型抗精神病薬に比べて錐体外路症状が少ないという利点がある一方で、代謝系副作用に関しては定型抗精神病薬よりも多いことが示唆されている。代謝系副作用は、心血管性あるいは脳血管性イベントの危険性に関連する。実際に、一般と比較して統合失調症をはじめとする重度の精神疾患患者の方が心血管性あるいは脳血管性イベントによる死亡率が高く、平均寿命が約 25 年短いことが報告されていることから、⁶⁾ 代謝系副作用は、錐体外路症状と同様に回避すべき重大な副作用である。

以上のことより、有効性および副作用の面から、非定型抗精神病薬が定型抗精神病薬よりも有用であると結論付けることはできず、非定型抗精神病薬が統合失調症治療における第一選択薬となっている現状の妥当性については、今後も検討していくべき課題として挙げられる。

3 治療抵抗性統合失調症の治療薬

いずれの抗精神病薬を使用しても十分に効果が認められない、治療抵抗性統合失調症の患者も少なくない。そこで近年注目されているのが、治療抵抗性統合失調症に対して有効性が確立しているクロザピンである。

治療抵抗性統合失調症とは、「数種類の抗精神病薬を十分な期間、十分な量投与したにもかかわらず、十分な反応が得られなかった統合失調症患者」と定義されている。クロザピンは様々な比較試験により、特に治療抵抗性統合失調症に対する治療効

果⁷⁾や自殺企図および自殺率の低下⁸⁾における有効性が報告されている。

クロザピンは非定型抗精神病薬の中でも初期に開発され、1969 年にオーストリアで承認されて以来、海外の様々な国で統合失調症の治療薬として使用されてきた。しかし、1975 年にフィンランドで 8 例の死亡例を含む 16 例の無顆粒球症の発現が報告されたことから、世界各国で一時期、開発・販売が中断されていた。1980 年代になって Kane ら⁹⁾により、治療抵抗性統合失調症に対するクロザピンの有効性が実証された。現在、クロザピンは、顆粒球減少の早期発見および無顆粒球症発現時に速やかな治療を目的とした血液モニタリングを義務付けた上で、治療抵抗性統合失調症を対象にした抗精神病薬として、世界 97 か国以上で承認を受けている。我が国でも 2009 年に発売され、施設基準を満たした病院で投与可能となった。

クロザピンの投与対象となる治療抵抗性統合失調症の指標として、「反応性不良」と「耐用性不良」があり、それぞれに基準が設けられている。反応性不良は、忍容性に問題がない限り、2 種類以上の十分量の抗精神病薬(クロルプロマジン換算で 600 mg/日以上、1 種類以上の非定型抗精神病薬を含む)を十分な期間(4 週以上)投与しても反応が認められなかった場合とされ、一方、耐用性不良は、非定型抗精神病薬のうち 2 種類以上による単剤治療を試みたが、中等度以上の遅発性ジスキネジア、遅発性ジストニア、あるいはその他の遅発性錐体外路症状の出現、または悪化もしくはコントロール不良のパーキンソン症状、アカシジア、あるいは急性ジストニアの出現などの理由により、十分な増量ができず、十分な治療効果が得られなかった場合とされている。

クロザピンの治療抵抗性統合失調症の改善率は、30% 程度であり、治療効果が期待される一方で、それでも改善しない症例群があることは明らかである。また、統合失調症における認知機能障害や陰性症状に対する薬物療法の有効性は、十分に実証されていない。現在の薬物療法の限界は、ドパミン仮説に基づいて開発された薬剤のみによる治療が行われていることに起因しており、近年では、グルタミン

酸受容体作動薬など新たな作用機序を有した薬剤の開発や治療応用が試みられている。⁹⁾

4 精神病未治療期間 (DUP) の短縮と前駆期への介入の意義

統合失調症の予後には、精神病未治療期間 (duration of untreated psychosis ; DUP) が大きく影響している。薬物療法の違いだけでなく、DUP の短縮もしくは統合失調症を発症する以前からの介入も重要視されている。

DUP とは一般に、陽性症状や一級症状の顕在化、すなわち「エピソードのはじまり」から、抗精神病薬による薬物療法や入院治療が開始されるまでの期間と定義されている。¹⁰⁾ DUP の長さとの予後の関連についてはこれまでに多数報告され、2005 年に発表された 2 つのメタアナリシス^{11,12)}においても DUP が長いほど予後が不良であり、短いほど良好であることが示唆された。このように治療開始の遅れが予後不良に繋がる要因として、発症後一定期間内の病態水準が長期化しやすいことや、精神病症状が進行性に脳の器質的変化に及ぼす影響が挙げられている。

Birchwood ら¹³⁾が提唱した治療臨界期仮説では、発症後 2 年以内における病態水準が長期に持続しやすく、発症後およそ 5 年以内の治療の成否が長期予後を決定的に上で重要であることが示唆されている。この治療臨界期仮説を検証するべく、Crumlish ら¹⁴⁾が DUP ならびに非特異的徴候が出現する前駆期を含めた罹病期間 (duration of untreated illness ; DUI) の長さ、4 年後、8 年後の転帰を調査した。その結果、図 1 のように DUI を 2 年以内と 2 年より長期に分けた場合、8 年後の機能の全体的評定 (the global assessment of functioning ; GAF) スコアは、DUI が 2 年以内の方が有意な差を持って改善を示している。また DUI が長期の群では、4 年後から 8 年後での改善が認められていない。このように、DUP だけでなく DUI も含めた早期の治療介入が長期予後に関連し、治療臨界期の存在を支持する結果が得られている。

統合失調症における MRI を中心とした脳の画像研究においては、発病後早期から顕著に生じる特定

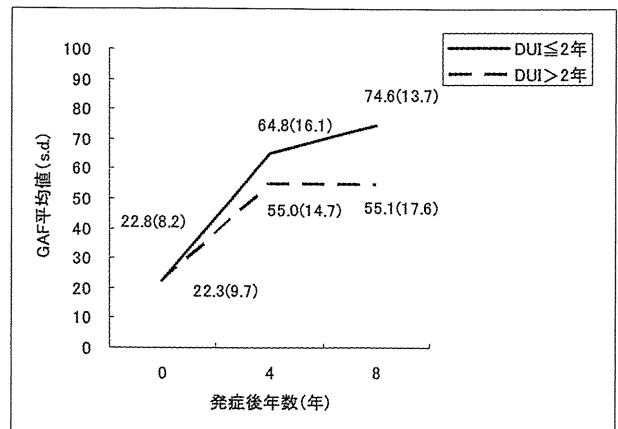


図 1 長期・短期 DUI 群と 0, 4, 8 年後の GAF 平均値 (文献 14 より引用)

領域の進行性の体積減少が報告されている。その要因としては、未治療の精神病症状が脳に及ぼす「生物学的毒性」の影響が示唆されている。^{15,16)} Cahn ら¹⁷⁾は、初回エピソード患者を対象に精神病症状の持続期間と 5 年後の頭部 MRI 上の変化を調べたところ、精神病症状の持続期間が長いほど有意に灰白質体積は減少し、脳室体積が増加していたことから、精神病症状と脳萎縮の関連性を報告している。また同様に、Lappin ら¹⁸⁾は DUP の長さが側頭葉の灰白質体積の減少に相関していることを報告している。

さらに統合失調症における進行性の脳形態変化に、抗精神病薬が影響を及ぼすことも示唆されている。抗精神病薬の使用と脳形態変化の関係性は、抗精神病薬、特に非定型抗精神病薬の神経保護作用が統合失調症の脳体積減少を阻止もしくは改善させる可能性が報告される一方で、抗精神病薬によって進行性に脳構造を変化させる可能性もあることが示唆されている。Ho ら¹⁹⁾は、統合失調症の脳構造変化に関与が予測される因子である罹病期間、抗精神病薬の使用、疾病重症度、薬物乱用歴と脳構造変化の関係を MRI を用いて調査したところ、抗精神病薬の使用期間の長さが他の 3 要因よりも強く、脳の灰白質、白質の体積減少に関与していたことを報告した。さらに興味深いことに、その結果は非定型抗精神病薬と定型抗精神病薬で差がなかった。統合失調症では、抗精神病薬が開始される以前である発症時点から既に脳体積が減少していることや、抗精神病

薬の使用が明らかに統合失調症の予後を改善することなどから、統合失調症の治療において抗精神病薬の使用を見合わせるべきだといった安易な結論に至ることはできないが、抗精神病薬の使用は必要最低限に抑えるべきであることが改めて示唆された。

Perkinsら¹⁹⁾は、DUPが短い群と長い群に分け、ハロペリドールとオランザピンによる比較研究を行った。その結果、DUPが短く病前機能が良好の群では、ハロペリドールとオランザピンのいずれにおいても効果の差がなく、治療反応性は良好であった。このことから、DUPが短ければ、非定型抗精神病薬だけでなく、定型抗精神病薬も有効であることが示唆された。筆者ら²⁰⁾の日本における調査では、DUPの長い群では短い群と比較して1年後の薬物量が多く、初回入院期間が長いという結果が得られている。これはDUPの長さが予後の悪化に繋がるとともに、抗精神病薬の治療反応性の悪化にも繋がることを示唆している。以上のことから、薬剤の種類よりもDUPの期間の方が、統合失調症の予後に大きく関与すること、またDUPを短縮することで、抗精神病薬の使用量の減量につながる可能性があることが示された。

また、これまでは顕在発症前の状態を後方視的に見て「前駆状態」としていたが、近年では、発症する危険のある精神状態を前方視的に同定し発症危険状態(at risk mental state; ARMS)と呼び、この期間から介入することの意義が強調され始めている。統合失調症を顕在発症する前から同定し、介入していく主な目的としては、統合失調症の発症を予防することや遅延させることが挙げられる。またたとえ発症したとしても、早期の段階での介入により、DUPを短縮させ予後の改善につながる。

実際にARMS群を対象とした抗精神病薬を用いた介入研究が行われ、^{21,22)} いずれも有意差までには至っていないが、抗精神病薬による効果が期待される結果が報告されている。その一方で、統合失調症発症前から抗精神病薬を使用することへの倫理的問題が発生することから、抗うつ薬や神経保護作用

が期待される物質を使用した介入研究も報告されている。

Ammingerらは、²³⁾ 神経保護作用が期待されサプリメントとしても使用されるオメガ3脂肪酸(ω -3 fatty acids)を使用し、プラセボを対象とした無作為二重盲検試験を行った。その結果、プラセボに対して ω -3 fatty acids使用群の方が有意に12か月間の精神病への移行率が低く、さらに副作用に関してはプラセボと差がなかったことが示された。今後の治療法として、期待される場所である。

5 おわりに

今なお、統合失調症のための新たな抗精神病薬の研究開発が行われている事実は、現在の抗精神病薬による治療に限界や課題があることを物語っている。現在の薬物療法の主な目的は症状の緩和であり、疾病の完治ではない。今後、統合失調症の根本治療を目指した新たな薬剤や更なる治療プログラムの研究開発が期待される場所である。

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サマリーシート

1. 対象者の年齢は 12 歳以上から 35 歳以下である： はい いいえ

2. 症状チェックリスト：

症状	あり	なし	症状の内容・出現時期・持続期間
感覚の変化			聴覚 / 視覚 / 触覚 / 嗅覚の異常
思考や発話の変化			奇異なアイデア, 猜疑心, 集中困難, 会話の脱線, 誇大性
機能の低下			仕事・学校での機能低下や社会的孤立
感情の変化			情動の平板化, 抑うつ気分, 不安感, 情緒不安, いらいら感
自律神経症状			睡眠困難, 食欲の変化, 身体愁訴
その他の変化			

まとめ

1. 症状チェックリストの結果から, 対象者には何らかの最近の変化を認める： はい いいえ
2. 対象者には知的能力の低下 (IQ 65 未満) が認められる： はい いいえ
3. 症状を説明しうるような何らかの神経疾患の既往がある： はい いいえ
4. 以前に精神病性障害の診断 / 治療を受けたことがある： はい いいえ

上記 1 に対する答えが「はい」で, 残りの答えが「いいえ」であれば, 評価の対象として適当であると判断する

付録 B

SIPS/SOPS 5.0

サイコーシス・リスクシンドロームに対する構造化面接
日本語版

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January 1, 2010

Version 5.0

サイコーシス・リスクシンドロームに対する 構造化面接

SIPS の概説

この面接の目的は以下の通りである：

- I. 過去あるいは現在の精神病状態を除外する
 - II. サイコーシス・リスクシンドロームの 3 つのタイプのうち 1 つ以上にあてはまるかを判断する
 - III. サイコーシス・リスク症状の現在の重症度を評価する
- I. 過去あるいは現在の精神病状態を除外する

過去の精神病状態は電話スクリーニングか被面接者の概観 (p236) から得られる情報を用いて除外され、精神病状態の診断基準 Presence of Psychotic Symptoms criteria (POPS) で評価される。

現在の精神病状態は陽性症状の有無によって定義される。現在の精神病状態を除外するためには 5 項目からなる陽性症状 (不自然な内容の思考 / 妄想, 猜疑心, 誇大性, 知覚の異常 / 幻覚, まとまりのないコミュニケーション) について質問し、評価する必要がある。

精神病状態の診断基準

精神病状態は以下のように定義される：

以下の (A) および (B) の両方を満たすことが必要である。

- (A) 以下の陽性症状が精神的なレベルで存在する (SOPS で 6 点のレベルに相当する)：
- ・不自然な内容の思考, 猜疑心 / 被害念慮, 誇大性が妄想的確信に基づいている
 - ・幻覚と呼ぶべき明らかな知覚の異常

- ・まとまりなく, およそ論理的でない発話
- (B) (A) に示した各症状が十分な頻度および期間, あるいは緊急性を備えていること：
- ・(A) の症状のうち少なくとも 1 つが 1 か月間に渡って, 最低でも平均週 4 回の割合で 1 日に 1 時間以上存在すること
- あるいは
- ・その症状が深刻であるか危険とみなされる場合

陽性症状はサイコーシス・リスク症状評価スケール Scale of Psychosis-risk Symptoms (SOPS) の P1 から P5 の項目で評価される。P1 から P5 のスケールで 1~5 点であれば陽性症状は非精神病性の強度であることが示唆される。P1 から P5 のスケールのうち 1 つ以上で 6 点であれば陽性症状が「重度かつ精神病性」の強度であることを意味しており, したがって上記 (A) に相当するとされる。

だが精神病状態が存在すると判断するには, (A) で示した症状の頻度と緊急性が十分に備わっている必要がある。もし陽性症状が上記 (B) の基準をも満たしていれば, 現在精神病状態にあると判断される。

II. サイコーシス・リスクシンドロームの 3 つのタイプのうち 1 つ以上にあてはまるかを判断する

(診断基準の要約は p296 を参照)

3 つのリスクシンドロームには, 各々相互に重複する可能性があることに注意が必要である。1 つのケースで同時に 2 つ以上のタイプのサイコーシス・リスクシンドロームを呈することがある。

過去あるいは現在の精神病状態の診断基準を満たさないケースに対しては, サイコーシス・リスクシンドロームの診断基準 Criteria of Psychosis-risk Syndromes (COPS) を用いて, 3 つのリスクシンドローム, すなわち短期間

の間歇的な精神病状態、微弱な陽性症状、遺伝的なリスクと機能低下を呈す群のうち1つかあるいはそれ以上に該当するかの評価が行われる。

サイコーシス・リスクシンドロームの診断基準(COPS)

A. 短期間の間歇的な精神病状態 Brief Intermittent Psychotic Syndrome (BIPS)

短期間の間歇的な精神病状態は、最近起きたきわめて短期間の明らかな陽性症状によって定義される。BIPSの基準を満たすためには、精神病レベル(SOPS 6点)の症状が過去3か月以内に始まり、かつ少なくとも1か月に1回の割合で1日に少なくとも数分間存在することが必要である。たとえ陽性症状が精神的なレベルで存在しているとしても(SOPS 6点)、それらが十分な頻度や期間、緊急性に対するPOPS(B)の基準を満たさないならば、現在の精神病状態からは除外できる。

B. 微弱な陽性症状 Attenuated Positive Symptom Syndrome(APS)

APSは十分な強度と頻度を備えた最近の微弱な陽性症状の存在によって定義される。微弱な症状の基準を満たすためには、SOPSのP1からP5までのスケールで3、4、5点のレベルにあることが必要とされる。症状がこの範囲に置かれることは、その強度がリスク状態のレベルにあることを示している。

また、その症状は過去1年間の間に始まったか、あるいは1年前に比べ現在少なくともスケール上で1点以上の上昇があることが必要とされる。さらに、過去1か月の間に少なくとも平均週1回の割合で現在のレベルでの症状の出現を認めることが必要である。

C. 遺伝的なリスクと機能低下

Genetic Risk and Deterioration Syndrome(GRDS)

GRDSは統合失調症圏の遺伝的リスクと最近の社会的機能の低下の併存によって定義される。一親等家族に精神病性障害(感情性精神病も含む)の家族歴がある場合、または本人がDSM-IVにおいて失調型パーソナリティ障害の診断を満たす場合に、遺伝的リスクが存在すると判断する。

機能低下の定義は、過去1か月の間のGAFスコアが最近1年間の最高レベルに比べ30%以上低下している場合に、操作的に適用する。

Ⅲ. サイコーシス・リスク症状の現在の重症度を評価する

サイコーシス・リスクシンドロームの少なくとも1つ以上のタイプに該当したケースに対し、SOPSを用いて陰性症状、解体症状、一般症状を評価する。ここで追加される情報はサイコーシス・リスクシンドロームの診断に寄与するものではないが、現在のサイコーシス・リスク症状の多様性と重症度に関して記述的かつ定量的な評価を与えることになる。したがって研究者によっては、あらゆるケースに対しすべてのSOPSを行うのが望ましいとする場合もある。

SIPS サイコーシス・リスクシンドローム基準の要約

I. 現在の精神病状態の除外(POPS)

精神病症状

- A. SOPS P1 から P5 スケールのうちどれか 1 つでも 6 点がありましたか？ はい いいえ
- B. 上記 A が該当した場合、その症状は深刻あるいは危険なものですか？ はい いいえ
- C. 上記 A が該当した場合、その症状は 1 か月に渡って少なくとも平均週 4 日の割合で 1 日に 1 時間以上認めますか？ はい いいえ

上記 A, B, C すべてに該当すれば、現在の精神病状態に相当する。
最初に基準に到達した日時(年月日)を記録： _____

II. サイコーシス・リスクシンドロームの検討(COPS3.0)

A. 短期間の間歇的な精神病状態

- 1. SOPS P1 から P5 スケールのうちどれか 1 つでも 6 点がありましたか。 はい いいえ
- 2. 上記 1 が該当した場合、その症状は過去 3 か月間に精神病的なレベルに達するものでしたか。 はい いいえ
- 3. 上記 1 および 2 が該当した場合、その症状は現在 1 か月に 1 回の割合で少なくとも数分の割合で存在するものですか。 はい いいえ

上記 1, 2, 3 すべて該当した場合、短期間の間歇的な精神病状態に相当する。
最初に基準を満たした日時(年月日)を記録： _____

B. 微弱な陽性症状

- 1. SOPS P1 から P5 スケールのうちどれか 1 つでも 3~5 点がありましたか。 はい いいえ
- 2. 上記 1 が該当した場合、それらの症状のうち 1 つでも 1 年以内に始まったかあるいは 1 年前に比べて 1 点以上上昇したのがありますか。 はい いいえ
- 3. 上記 1 および 2 が該当した場合、その症状は過去 1 か月間で少なくとも平均週 1 回の割合で存在するものですか。 はい いいえ

上記 1, 2, 3 すべて該当した場合、微弱な陽性症状の基準を満たす。
最初に基準を満たした日時(年月日)を記録： _____

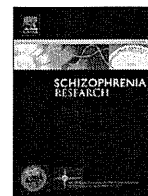
C. 遺伝的なリスクおよび機能の低下

- 1. 失調型パーソナリティ障害の診断基準を満たしますか。 はい いいえ
- 2. 精神病性障害を持つ一親等家族が存在しますか。 はい いいえ
- 3. 最近 1 か月間の GAF の値が 1 年前に比べ少なくとも 30% 以上低下していますか。 はい いいえ

上記 1 および 3、または 2 および 3、あるいは 1~3 までの全てを満たす場合に、遺伝的なリスクおよび機能の低下が存在すると診断される。
最初に基準を満たした日時(年月日)を記録： _____

以下該当するものに○をつけてください。

精神病状態 _____
 短期間の間歇的な精神病状態 _____
 微弱な陽性症状 _____
 遺伝的なリスクと機能の低下 _____
 他の精神疾患 DSM における I 軸疾患 _____ II 軸疾患 _____



Lack of association between psychosis-like experiences and seeking help from professionals: A case-controlled study

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ABSTRACT

Backgrounds: It still remains unclear whether individuals who experience attenuated psychotic symptoms are likely to seek help, whereas depressive symptoms are more likely to be associated with help-seeking behavior than these symptoms themselves. The aims of our study were to compare the profile of these symptoms between clinical and community samples and to investigate to what extent help-seeking behavior depends on the severity of psychosis-like symptoms and/or depressive symptoms.

Methods: The clinical sample consisted of help-seeking outpatients aged 16–30 years who had approached a community mental health clinic (N = 750, mean age: 23.3 ± 4.2 years, 62.4% females). The community sample was comprised of students from two universities and two high schools (N = 781, mean age: 18.1 ± 1.7 years, 59.2% females). Psychosis-like experiences were assessed using the PRIME Screen-Revised (PS-R), a self-reported screening instrument for assessing the risk of psychosis. Depressive symptoms were assessed using the Zung Self-rating Depression Scale (ZSDS), a 20-item self-reported questionnaire.

Results: Among the clinical and community samples, 27% and 10% had positive PS-R results respectively. No significant difference in the PS-R total score or the frequency of PS-R-positive items was observed between the clinical and community samples. A logistic regression analysis revealed that none of the psychosis-like experiences were significantly associated with help-seeking behavior, after controlling for the effect of depressive symptoms.

Conclusions: Our findings showed that attenuated psychotic symptoms do not contribute significantly to help-seeking behavior, suggesting that the relationships among PLEs, depressive symptoms, and help-seeking behavior should be reconsidered.

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1. Introduction

Recent growing interest in early detection and intervention for psychosis has shifted to include the care of individuals with an at-risk mental state—mostly those with help-seeking behavior. However, whether individuals who experience attenuated psychotic symptoms are likely to seek help remains unclear. Whereas several studies have demonstrated that these symptoms or psychotic-like experiences (PLEs) were associated with distress or help-seeking behavior in both community (Armando et al., 2010; Murphy et al., 2010) and clinical samples (Yung et al., 2006), not a few studies have revealed that these experiences are frequent phenomena and thus are not necessarily associated with distress or seeking help (Hanssen

et al., 2003; Dominguez et al., 2009; van Os et al., 2009). Moreover, multiple studies have indicated that untreated mental disorders are highly prevalent among student populations (Hunt and Eisenberg, 2010); this is consistent with the general population, in which a median delay of 11 years was noted between the onset of illness and presentation for treatment (Wang et al., 2005). These findings indicate the possibility that help-seeking subjects with attenuated psychotic symptoms or PLEs do not represent the entire sample that will actually develop subsequent psychosis. Indeed, a recent retrospective study on first-episode psychosis showed that fewer than one in five people initiated help-seeking behavior by themselves during the prodromal phase (O'Callaghan et al., 2010). Given that some PLEs or attenuated psychotic symptoms confer an increased risk of developing severe mental disorders in clinical and community samples (Poulton et al., 2000; Cannon et al., 2008), restricting study samples to subjects with help-seeking behavior or clinical samples might not be sufficient to investigate the developmental process of psychosis. As such, differences in the PLE profiles

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or attenuated psychotic symptoms between clinical samples and non-clinical samples should be clarified.

Studies on the association between PLEs and distress have also shown a significant association between PLEs and depression (Yung et al., 2006), suggesting that depressive symptoms may influence emerging distress or help-seeking behavior among individuals with PLEs. Depressive symptoms were among the most frequent early signs described by patients who had recently experienced their first episode of psychosis (Häfner et al., 2005). In a study that included adolescents “at imminent risk for psychosis,” the most common diagnosis of the study participants according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) was major depression (Meyer et al., 2005). In addition, several general population studies have demonstrated that distress and depression are major factors in determining whether people with PLEs require specialist psychiatric help (Bak et al., 2003, 2005; Hanssen et al., 2005).

Within this context, depressive symptoms are more likely to be associated with help-seeking behavior than attenuated psychotic symptoms or PLEs; thus, help-seeking subjects with PLEs may represent a more depressed sample, compared with the entire sample of subjects developing subsequent psychosis. Meanwhile, if the elevated level of PLEs genuinely leads to help-seeking behavior, the severity of the PLEs would likely be higher among help-seeking subjects than among non-help-seekers, and the subjects experiencing attenuated psychotic symptoms would likely seek help regardless of the severity of their depressive symptoms.

In the current study, we sought to test our hypothesis that help-seeking behavior in individuals with attenuated psychotic symptoms would be associated with depressive symptoms but not with the presence or severity of PLEs. Therefore, we aimed to compare clinically help-seeking subjects with PLEs and community non-help-seeking subjects with PLEs. Throughout this study, we have used the term ‘help-seeking’ to refer to individuals seeking help from psychiatric professionals and ‘clinically help-seeking subjects’ to refer to individuals who approached a community mental health clinic by themselves.

The aims of our study were (i) to compare the profile of PLEs between clinical and community samples, and (ii) to investigate to what extent help-seeking behavior depends on the severity of psychosis-like symptoms and/or depressive symptoms.

2. Methods

2.1. Participants

The study subjects were comprised of clinical and community samples.

The clinical sample consisted of help-seeking outpatients aged 16–30 years who had approached a community mental health clinic (Shakujii-Kouen Clinic, located in a suburb of Tokyo) for the first time between December 2006 and September 2008. This clinic primarily provides care for common mental illnesses with onsets at all age, including depression, anxiety disorders, or dementia; in other words, the clinic does not provide specialized care for psychosis-risk populations. All the outpatients in the age group of interest that attended this clinic during the timeframe (between December 2006 and September 2008) were given self-reported questionnaires prior to undergoing a clinical examination at the time of their presentation. After excluding those individuals who were clearly reluctant to seek help (e.g., after involuntary contact with police or emergency services) ($N = 8$), a total of 750 outpatients were enrolled in this study (mean age: 23.3 ± 4.2 years). The sample included 282 males (37.6%) and 468 females (62.4%).

The community sample was comprised of students from two universities and two high schools. The students were given self-

reported questionnaires at the beginning of a class without any advance information regarding psychiatric disorders or related symptoms. All the participants provided their informed consent and had the right not to answer any of the questions. A total of 781 students were enrolled in the present study (496 university students and 285 high school students; mean age: 18.1 ± 1.7 years). The sample included 319 males (40.8%) and 462 females (59.2%).

Either an ethical meeting or the Institutional Review Board at each site approved the study protocol and the informed consent procedures.

2.2. Measures

2.2.1. Psychosis-like experiences or attenuated psychotic symptoms

Psychosis-like experiences were assessed using the PRIME Screen-Revised (PS-R), a self-reported screening instrument (Kobayashi et al., 2008). The original PRIME Screen, developed by Miller et al. at the PRIME clinic in New Haven, CT, USA, is a screening instrument for assessing the risk of psychosis (Miller et al., 2004). The questionnaire is based on items from the Structured Interview for Prodromal Syndromes (SIPS), which was also developed by Miller et al. (2003). This screening questionnaire consists of 11 items covering positive symptoms (delusional mood, overvalued belief, ideas of passivity, magical thinking, derealization, telepathy-like experiences, ideas of reference, increased self-esteem, perceptual distortions, any auditory hallucinations, and thought hearing) and an item referring to insight into illness. These 12 items are self-rated using a scale of 0 (definitely disagree) to 6 (definitely agree). A score of 4 (slightly agree) was regarded as a “positive” endorsement.

Based on this original PRIME Screen, we had previously developed the PS-R by adding a question to the PRIME Screen concerning how long the change in function, behavior or thought had been apparent (such as less than 1 week, between 1 week and 1 year, or more than 1 year). The participants were classified into 11 ranks (from 0 to 10) based on a combination of the rating of symptoms, the duration of symptoms, and the total score on the PS-R. The last item of the PS-R refers to ‘insight into illness’ (“I have been concerned that I might be ‘going crazy’”), which was not derived from the SIPS and was not related to attenuated positive symptoms; therefore, the response to the 12th item was not taken into account at the time of the evaluation. We had tested the clinical validity of the PS-R by comparing a non-clinical population (496 students) with a clinical population (528 outpatients) (Kobayashi et al., 2008). If subjects with a rank of 4 or greater were regarded as positive, the specificity and sensitivity of the PS-R using the SIPS as a gold standard were 0.74 and 1.00, respectively. The concordant validity between the PS-R and the SIPS was 0.43. Thus, in this study, we considered subjects with a rank of 4 or greater as being positive.

2.2.2. Depressive symptoms

Depressive symptoms were assessed using the Zung Self-rating Depression Scale (ZSDS), a 20-item self-reported questionnaire (Zung and Durham, 1965). The ZSDS was developed to measure the cognitive, emotional, and physical symptoms associated with depression, and has been established as a valid, reliable measure of depression. The items are rated using a 4-point Likert scale ranging from 1 (rarely) to 4 (most of the time), with higher scores corresponding to a greater severity of depressive symptomatology.

2.3. Data analysis

Given the difference in age between the groups, we split the clinical screening positive group into an age-matched group (age range: 16–21 years) and the remaining group (age range: 22–30 years). We then compared the demographic and clinical variables for the positively screened individuals with those for the clinical, age-

matched clinical, and community groups using the analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Post-hoc comparisons were performed to test the differences between the clinical and community groups using the Bonferroni test to adjust the observed significance level for multiple comparisons. The Kruskal–Wallis H-test was conducted to evaluate the difference of the PS-R rank distributions among groups.

To explore to what extent help-seeking behavior depended on psychosis-like experiences and/or depressive symptoms, a logistic regression analysis was conducted. Then, to test the hypothesis that help-seeking behavior would be independent of psychosis-like experiences, a second logistic regression analysis controlling for the effect of depressive symptoms was conducted.

All of the statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). A two-tailed p -value < 0.05 was considered to be statistically significant.

3. Results

Of the 750 psychiatric outpatients (clinical sample or help-seeking group), 731 subjects (97.5%) agreed to participate and completed the questionnaires, 4 (0.5%) declined to answer the questionnaires, and 15 (2.0%) could not understand the instructions or the meaning of the questions. Of the community sample (781 students; non help-seeking group), 748 (95.8%) completed the questionnaires. The current study examined data obtained from these 731 outpatients (mean age: 23.3 ± 4.2 years; female: 64.0%) and 748 students (mean age: 18.1 ± 1.7 years; female: 60.8%).

Among the clinical sample ($n = 731$), 199 (27%) had positive PS-R results, whereas among the non-help-seeking subjects ($n = 748$), 82 (10%) had positive PS-R results. A significant difference in the prevalence of PS-R positives was observed between the clinical and community samples ($\chi^2 = 69.00$, $df = 1$, $p < 0.01$). The demographic variables and the profile of symptoms for the PS-R-positive group are summarized in Table 1. Although significant differences in some PS-R items (clinical > community: ideas of passivity, ideas of reference, perceptual distortions, insight into illness) and the ZSDS total score were observed, no significant difference in the PS-R total score or the

frequency of PS-R-positive items was observed between the clinical and community samples. Regarding the rate of subjects who endorsed the PS-R “definitely agree” item with a duration longer than 1 year, the community PS-R-positive group had a higher rate than the clinical groups. Similarly, no differences in the distribution of the PS-R rank were observed between the clinical PS-R-positive groups and the community PS-R-positive sample ($\chi^2 = 1.024$, $df = 3$, $p = 0.795$, Kruskal–Wallis, H) (see Table 2).

A logistic regression analysis to explore the extent to which help-seeking behavior depends on psychosis-like experiences and/or depressive symptoms revealed that none of the psychosis-like experiences were significantly associated with help-seeking behavior, after controlling for the effect of depressive symptoms (see Table 3). An analysis using an age-matched clinical sample ($n = 157$) yielded the same results (Table 3). On the other hand, the ZSDS total score contributed significantly to the help-seeking behavior.

4. Discussion

The main finding in the current study is that PLEs or attenuated psychotic symptoms do not contribute significantly to help-seeking behavior, as hypothesized. Understanding what this result implies may require some clinical investigation.

In general, the backgrounds of subjects who do not seek help from professionals can include personal barriers (lack of time, privacy concerns, and financial constraints) and/or common barriers (the lack of a perceived need for help, being unaware of services or insurance coverage, and skepticism regarding the effectiveness of treatment) (Eisenberg et al., 2007; Hunt and Eisenberg, 2010), suggesting that distress or subjective difficulties may overwhelm these barriers when the apparent help-seeking behavior emerges. Although it is difficult to draw conclusions because this study did not assess these personal/common barriers, PLEs or attenuated psychotic symptoms are less likely to be associated with distress or subjective difficulties than depressive symptoms. In some cases, therefore, the attenuated psychotic symptoms may become more persistent and prevalent beyond the threshold of psychosis before the onset of help-seeking behavior. Some retrospective studies imply that a considerable proportion of psychotic patients experience their first episodes prior to

Table 1
Demographic variables and the profile of symptoms for each PS-R positive groups.

Variable	Clinical PS-R+		Community PS-R+ (N = 82)	Overall F, χ^2	p
	All (N = 199)	Age-matched (N = 75)			
Gender, female; n (%)	128 (64.3)	47 (62.7)	42 (51.2)	3.5	0.170
Age, years; mean (SD)	22.6 (4.2)**	18.2 (1.7)	18.0 (1.8)	58.9	<0.001
PS-R item; mean (SD)					
Delusional mood	3.1 (2.2)	2.9 (2.2)	2.4 (2.0)	2.9	0.057
Overvalued belief	2.0 (1.9)	1.8 (1.8)	2.1 (2.0)	0.5	0.620
Ideas of passivity	4.2 (2.1)	4.2 (2.0)	3.5 (2.20)	3.6	0.028
Magical thinking	2.4 (2.1)	2.3 (2.1)	2.6 (2.1)	0.5	0.617
Derealization	3.4 (2.2)	3.4 (2.3)	2.7 (2.2)	3.1	0.046
Telepathy-like experiences	4.2 (2.0)	3.9 (1.9) †	4.8 (1.7)	4.1	0.018
Ideas of reference	4.1 (2.0)	4.0 (2.2)	3.2 (2.2)	4.9	0.008
Increased self-esteem	2.0 (2.1)	1.9 (2.1)	2.4 (2.3)	6.2	0.333
Perceptual distortions	3.2 (2.3)	3.3 (2.2) **	2.2 (2.3)	6.2	0.002
Any auditory hallucinations	2.7 (2.3)	3.0 (2.3)	2.2 (2.4)	2.3	0.106
Thought hearing	2.6 (2.1)	2.8 (2.1)	2.0 (2.1)	3.0	0.052
Insight into illness	4.8 (1.6) **	4.9 (1.7) **	3.9 (1.9)	7.4	0.001
PS-R total score; mean (SD)	33.6 (12.0)	33.1 (12.2)	30.0 (12.2)	2.7	0.070
Frequency of PS-R positive items; mean (SD)	5.2 (2.4)	5.1 (2.4)	4.7 (2.3)	1.7	0.190
PS-R severe items +; n (%)	119 (59.8) ††	40 (53.3) ††	64 (78.1)	11.8	0.003
ZSDS total score; mean (SD)	57.1 (8.4) **	57.2 (8.8) **	44.6 (9.2)	65.9	<0.001

Note: PS-R: the PRIME Screen-Revised, ZSDS: the Zung Self-rating Depression Scale.

Statistic value is F for continuous variables and χ^2 for categorical variables.

Mean value was significantly higher than that of the community PS-R+ group: * $p < 0.05$, ** $p < 0.01$ (Bonferroni corrected).

Mean value or number was significantly lower than that of the community PS-R+ group: † $p < 0.05$, †† $p < 0.01$ (Bonferroni corrected).

Table 2
Prevalence of the PS-R rank among PS-R+ samples.

Rank	Definition	All PS-R+ (n = 281)	Clinical PS-R+ (n = 199)	Age-matched Clinical PS-R+ (n = 75)	Community PS-R+ (n = 82)
		n (%)	n (%)	n (%)	n (%)
10	Selected three or more "definitely agree" responses with durations of more than one year	47 (17)	31 (16)	10 (13)	16 (20)
9	Selected two "definitely agree" responses with durations of more than one year and one or more "somewhat agree" response with a duration of more than one year	32 (11)	24 (12)	8 (11)	8 (9.8)
8	Selected two "definitely agree" responses with durations of more than one year or selected two or more "definitely agree" responses without regard to the duration and one or more "somewhat agree" response with a duration of more than one year	23 (8.2)	18 (9.1)	7 (9.3)	5 (6.1)
7	Selected one "definitely agree" response with a duration of more than one year and one or more "somewhat agree" response with a duration of more than one year	36 (13)	25 (13)	9 (12)	11 (13)
6	Selected two or more "definitely agree" responses without regard to the duration or selected three or more "somewhat agree" responses with durations of more than one year	58 (21)	47 (24)	16 (23)	11 (13)
5	Selected one "definitely agree" response with a duration of more than one year or selected two "somewhat agree" response with durations of more than one year	82 (29)	53 (27)	24 (32)	29 (35)
4	Have a total PS-R score of 39 or over	3 (1.1)	1 (0.5)	1 (1.3)	2 (2.4)

apparent help-seeking behaviors (Addington et al., 2002; O'Callaghan et al., 2010). Our findings may partly support this outcome, since the results showed that the PLEs in the non-help-seekers were no less severe than those in help-seekers.

Another clinical implication is that our results suggest that some psychosis-like symptoms may underlie the appearance of depressive symptoms; these experiences might easily be hidden and therefore often cannot be identified, even in subjects with help-seeking behavior. Moreover, subjects experiencing PLEs may not necessarily recognize the 'real' nature of their attenuated psychotic symptoms. For example, a female college student with a persecutory idea reports that she is always being watched by someone, but simultaneously does not consider this experience to be a 'symptom'. Though she may be aware of distress, anxiety or depressive symptoms, she may be unaware of the psychosis-like nature of these symptoms. Given that psychosis-like symptoms confer an increasing risk of the onset of psychosis, especially when comorbid with depressive symptoms, greater clinical effort should be made to detect these attenuated symptoms and to inform subjects of their significance.

Our findings regarding the prevalence of subjects with psychosis-like symptoms in a community mental health clinic may also provide valuable information for primary mental health services. Whereas numerous studies have examined the prevalence of PLEs in general populations, only a few studies have reported the prevalence of psychosis-risk subjects among clinical populations. Our results indicating that over 20% of the clinical help-seekers endorsed some psychosis-risk symptoms may be somewhat higher than expected,

since a recent review on the subclinical psychotic experience revealed a prevalence in general populations of around 5% (van Os et al., 2009). The pathways to care of patients with early psychosis may differ depending on the first contact (Anderson et al., 2010), suggesting that a cautious first contact may lead to a successful early intervention. Thus, it is of great significance that these potential risk symptoms be assessed accurately by community mental health services.

The present study had some limitations. First, the reliability of the self-reported symptoms remains somewhat uncertain. In addition, almost all the information was obtained from the patients themselves. We should consider the possibility that young participants may often misunderstand the questions or interpret them in unintended ways. Secondly, we have little detailed information on the help-seeking behavior of the subjects. We have no data on the degree to which the subjects needed help or whether the subjects or their family members sought help. Although help-seeking behavior cannot be easily quantified or objectified (Gladstone et al., 2007), we should consider this limitation as a methodological weakness. Thirdly, no information was available regarding whether the community sample had any history of visits to psychiatric services. In particular, if the students with more severe PLEs had sought help from professionals, the results would be changed. However, more subjects in the community PS-R-positive group responded negatively to the item regarding 'insight into illness' ("I have been concerned that I might be 'going crazy'") than in the clinical PS-R-positive group (Table 1), suggesting that only a small percentage of the community PS-R-positive subjects, if any, had sought care from professionals. Lastly, as mentioned above,

Table 3
Logistic regression analysis examining association between PS-R item score and help-seeking behavior.

PS-R item	All PS-R+ (n = 281)				Age-matched PS-R+ (n = 157)			
	Unadjusted		Adjusted ^a		Unadjusted		Adjusted ^a	
	OR	(95% C.I.)	OR	(95% C.I.)	OR	(95% C.I.)	OR	(95% C.I.)
Delusional mood	1.16*	(1.03–1.31)	1.06	(0.91–1.22)	1.12	(0.96–1.30)	1.00	(0.83–1.21)
Overvalued belief	0.96	(0.84–1.10)	1.06	(0.89–1.26)	0.93	(0.79–1.10)	1.06	(0.85–1.32)
Ideas of passivity	1.17*	(1.04–1.32)	1.01	(0.86–1.19)	1.20*	(1.01–1.41)	1.04	(0.84–1.29)
Magical thinking	0.95	(0.84–1.08)	0.86	(0.73–1.00)	0.93	(0.80–1.08)	0.87	(0.72–1.06)
Derealization	1.15*	(1.02–1.29)	0.87	(0.74–1.02)	1.17*	(1.01–1.36)	0.90	(0.74–1.10)
Telepathy-like experiences	0.85*	(0.73–0.99)	0.86	(0.72–1.03)	0.78**	(0.65–0.93)	0.87	(0.72–1.03)
Ideas of reference	1.20**	(1.06–1.35)	0.95	(0.82–1.11)	1.17*	(1.01–1.35)	0.89	(0.73–1.09)
Increased self-esteem	0.93	(0.82–1.04)	1.05	(0.90–1.22)	0.91	(0.79–1.05)	1.00	(0.83–1.20)
Perceptual distortions	1.21**	(1.08–1.36)	1.00	(0.87–1.16)	1.24**	(1.07–1.43)	1.04	(0.87–1.24)
Any auditory hallucinations	1.09	(0.97–1.22)	0.98	(0.85–1.12)	1.16*	(1.01–1.33)	1.04	(0.88–1.24)
Thought hearing	1.14*	(1.00–1.29)	0.99	(0.84–1.15)	1.20*	(1.03–1.40)	1.04	(0.85–1.26)
Insight into illness	1.31**	(1.11–1.52)	1.00	(0.82–1.22)	1.36**	(1.11–1.67)	1.04	(0.81–1.33)

Note: PS-R: the PRIME Screen-Revised, ZSDS: the Zung Self-rating Depression Scale.

^a Adjusted for ZSDS total score.

* p < 0.05.

** p < 0.01.

the present study did not assess the personal/common barriers for help-seeking behavior. If such data were available, our hypothesis regarding the attenuated psychotic symptoms and help-seeking behavior would be more robust.

In spite of these limitations, our findings shed new light on community-based interventions for subjects at risk for the onset of psychosis. Now that attenuated psychotic symptoms or PLEs appear to not be associated with help-seeking behavior, we should reconsider these psychosis-risk-positive subjects as a heterogeneous sample. A recent systematic review on the pathways to care underlined the complexity of the issue of help-seeking behaviors among subjects with early psychosis (Anderson et al., 2010). Further longitudinal studies, including studies examining the phase after the onset of psychosis, are required to clarify the relationship among attenuated psychotic symptoms, depressive symptoms, and help-seeking behaviors.

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Contributors

Hiroyuki Kobayashi and Masafumi Mizuno designed the study and wrote the protocol. Takahiro Nemoto and Haruo Kashima were involved at the conceptualization level of the project. Masaaki Murakami and Hiroyuki Kobayashi collected the data. Hiroyuki Kobayashi analyzed and interpreted the data and wrote the first draft of this manuscript. Masafumi Mizuno contributed to the writing, editing and revision of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Regular Article

Successful aging in individuals with schizophrenia dwelling in the community: A study on attitudes toward aging and preparing behavior for old age

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Aim: ‘Successful aging’ in individuals with schizophrenia has been attracting attention. We examined two forward-looking factors of successful aging among schizophrenia patients: ‘attitude toward aging’ and ‘preparing behavior for old age’.

Methods: Fifty-seven middle-aged and elderly schizophrenia patients with successful aging were identified using the Attitude toward Aging Scale, the Preparing Behavior for Old Age Scale, and assessments of their cognitive function, psychiatric symptoms, social functioning and quality of life. A multiple regression analysis was used to detect determinants of attitude toward aging/preparing behavior for old age at that time (‘present’: community dwelling). We also analyzed predictors of successful aging using demographic/clinical data assessed 3 years previously (‘past’: residential care).

Results: The multiple regression analysis revealed that quality of life was a significant determinant: a

higher quality of life was related to a more positive attitude toward aging and less active preparing behavior. The significant predictors of preparing behavior were quality of life and the length of the hospital stay: a longer hospital stay and a higher quality of life were related to less active preparing behavior.

Conclusion: Quality of life and the length of the hospital stay significantly contributed to forward-looking factors of successful aging. Avoiding long hospitalization periods for patients with schizophrenia may lead to more active preparing behavior, but the improvement of quality of life may not be a sufficient condition. As schizophrenia patients have an optimistic attitude and insufficient preparing behavior, support to prepare such individuals for old age is required as part of community-based psychiatric care strategies.

Key words: community, deinstitutionalization, quality of life, schizophrenia, successful aging.

THE CIRCUMSTANCES OF psychiatric care have changed considerably globally. Long-term hospital treatments have been replaced by community-based services that focus on supporting independent daily life and employment. Meanwhile, psychiatric

services still remain predominantly hospital-based in Japan. A decline in hospital beds has been observed since 1994, but the total number of inpatient beds is still much larger (2.7 per 1000 people) than the numbers in the UK and the USA (0.7 and 0.3, respectively).¹

The earliest large-scale project to enable a total transition from a psychiatric hospital to a residential facility in Japan was established in 2002 and was known as the Sasagawa Project, held in Koriyama, Fukushima.^{2,3} During the first stage of the project, 78

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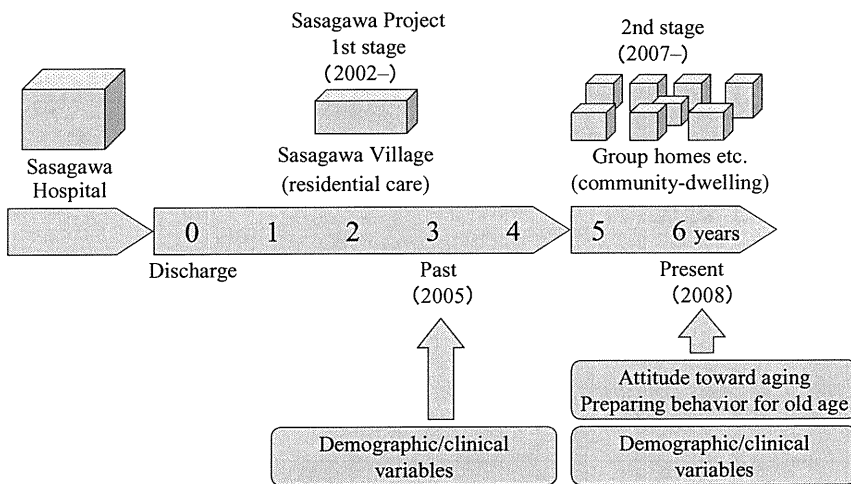


Figure 1. Progress of the Sasagawa Project and assessment of successful aging and other factors.

patients with schizophrenia who had been inpatients at Sasagawa Hospital for long time periods underwent 1 year of psychosocial training according to the protocol outlined by the Optimal Treatment Project (OTP).^{4,5} The patients were then discharged from the mental hospital and transferred to a supported residential facility, called Sasagawa Village, following the closure of the hospital in March 2002. During the second stage, the patients gradually left the residential facility and moved into the neighboring community in 2007, where they mainly lived in 19 group homes and several apartment houses (Fig. 1). They attended a day-care center, a community care support center, and the ‘I Can’ program and received nursing care visits. Some of the patients began supported job training. However, even though the patients had resumed their own daily living activities, they were already approaching old age. Thus, ‘successful aging’ may be a key concept in their community-based psychiatric care.

The concept of successful aging has grown in sociology, and it emphasizes that growth during senescence is more important than the decline caused by aging. Successful aging is influenced by lifestyle, rather than inherited characteristics, and it is a multidimensional concept that includes physical, psychological and social environmental factors.⁶ That is to say, successful aging is a bio-psycho-social adaptation to the changes that occur during aging.

Although aging with chronic diseases has been considered as pathological aging in the field of medicine and age-related function declines as during normal aging, Rowe and Kahn advocated dividing normal aging into usual and successful aging: indi-

viduals belonging to the former category showed typical non-pathologic and age-linked losses, while those belonging to the latter category showed fewer or no functional losses.⁷ They defined successful aging according to three main components: low probability of disease and disease-related disability, high cognitive and physical capacity, and active engagement with life.⁸

Several studies have been conducted since Rowe and Kahn’s study. Depp *et al.* reported that although no consensus exists for the definition of successful aging, most of the definitions of successful aging included components that could be described as disability/physical functioning, cognitive functioning, life satisfaction/well-being, and social/productive engagement.^{9,10} Vaillant *et al.* suggested that successful aging in an individual’s seventies could be predicted by variables assessable before the age of 50.¹¹ Baltes *et al.* demonstrated greater functional losses of everyday functioning in the non-successful aging group than in the successful aging group.¹² Cohen *et al.* demonstrated that older outpatients with schizophrenia showed favorable outcomes upon symptom remission (49%) but lower favorable levels upon community integration (23%) and for subjective (13%) and objective (2%) successful aging, compared with similarly aged peers.¹³

Although some previous medical studies have examined successful aging, few studies have used a subjective definition of successful aging¹⁴ or have dealt with the successful aging of individuals with schizophrenia. Previous studies on successful aging have mainly examined the existing condition at that time-point. The measures of successful aging were

also simple and fundamental in the previous studies.

The selective optimization with compensation (SOC) model for successful aging focuses mainly on how people optimize resources and aids that facilitate success and compensate for losses to adapt to changes throughout their lives and to create an environment for lifelong successful development. In the SOC model, Ouwehand *et al.* argued that proactive coping aimed at preventing potential threats to goals is important for successful aging.¹⁵

The present study focuses on two forward-looking factors of successful aging in individuals with schizophrenia: 'attitude toward aging' and 'preparing behavior for old age'. The 'attitude toward aging' factor refers to a subjective awareness of one's forthcoming later life and is based on the expected social situation and the prospects of one's own aging.¹⁶ To prepare for the achievement of a satisfactory and suitable later life, coping with the aging process should start during middle age. The 'preparing behavior for old age' factor refers to voluntary and objective conduct that is performed to prepare for various difficulties during one's old age.¹⁷ Having a proper perspective on old age seems to be an important factor in the successful aging of individuals with schizophrenia living in the community. To identify means of supporting such individuals, researchers must be aware of the attitude of these patients toward aging and their preparing behavior for old age. However, these issues have not been widely studied in individuals with schizophrenia.

In this study, we first examined successful aging in individuals with schizophrenia using the two forward-looking factors mentioned above. Second, we identified the determinants of the present and predictors at the past points and ascertained the change in patients after transitioning from residential facility care to community dwelling, which influenced the attitudes toward aging and preparing behavior.

METHODS

Subjects

The subjects consisted of 57 individuals with schizophrenia (37 men and 20 women). The mean age was 59.7 years (SD = 6.9) and their mean number of years of education was 10.6 (SD = 2.0). Seventeen patients of the 57 had been married. Their mean

duration of illness was 36.5 years (SD = 8.1), and their mean age at onset was 23.2 years old (SD = 5.6). All the subjects were diagnosed using the ICD-10¹⁸ as having chronic schizophrenia by two independent psychiatrists. All the individuals were being treated with antipsychotics, with a mean chlorpromazine-equivalent dose of 823.3 mg/day (SD = 443.2): 34 patients had been treated with only second-generation antipsychotic drugs, 19 patients had been treated with only first-generation drugs and four patients had been changed from one type to the other type of drugs at past and present assessment points. Fifty individuals were living in small-scale psychiatric group homes, and seven individuals lived in personal residences.

None of the subjects had a history of alcoholism, drug abuse, or serious neurological illness. As most of the subjects in this study received equal public economic support (disability pension and livelihood protection), their economic status was almost equal. Therefore, we did not take economic factors into account in this study.

The institutional review board of the Asaka Hospital approved the protocol of the study. The study was carried out in accordance with the latest version of the Declaration of Helsinki. After providing the subject with a complete description of the study, written informed consent was obtained from every subject.

Procedures

We assessed attitude toward aging and preparing behavior for old age as well as cognitive function, psychiatric symptoms, social functioning and quality of life (QOL) in 2008 ('present': after the transition to community dwelling). We also used demographic/clinical data assessed 3 years earlier, in 2005 ('past': during residential care) (Fig. 1).

The Attitude toward Aging Scale was developed to assess the awareness of one's later life and is a representative scale for measuring forward-looking factors of successful aging in Japan.¹⁶ This scale is composed of the following ten questions: (i) anxiety for health in old age; (ii) relationship with the younger generation; (iii) provision for social welfare and guarantee system; (iv) maintenance of health; (v) economic stability; (vi) independent life; (vii) social activity; (viii) solidarity with the younger generation; (ix) spiritual vitality/keeping one's youth; and (x) a fulfilling life. Each question in the scale is composed of a pair of choices that are considered avoiding value

judgments. Each question is rated using a 2-point scale (positive = 1, negative = 0). A higher score indicates a higher degree of positive attitude toward aging. The total score for the 10 questions was used in this study.

The Preparing Behavior for Old Age Scale¹⁷ is composed of the following five questions: (1) Do you save money for a stable old life? (2) Do you maintain a regular life or exercise to maintain your health? (3) Do you find your life worth living through the enjoyment of hobbies or social activities? (4) Do you have many social contacts with your friends or neighbors? (5) Do you maintain a peaceful family relationship? Each question is rated using a 3-point scale (making considerable effort = 3, to some degree = 2, not at all = 1). Higher scores indicate higher degrees of active preparing behavior. The total score for the 5 questions was calculated.

The total number of hospitalized days for each individual was determined by consulting each patient's medical records.

The Mini-Mental State Examination (MMSE) was used to assess general cognitive capacity.¹⁹ The Positive and Negative Syndrome Scale (PANSS)^{20,21} was used to obtain scores for the positive symptom, negative symptom, and general psychopathology subscales. The Global Assessment for Functioning (GAF)²² was used to measure global social functioning, and two other scales were used to measure community functioning: the Rehabilitation Evaluation Hall and Baker Scale (REHAB),^{23,24} and the Social Functioning Scale (SFS).^{25,26} The 26-item short form of the World Health Organization Quality of Life scale (WHOQOL26) was used and the average score was adopted.²⁷

Statistical analysis

All statistical analyses were performed using SPSS 17.0. Initially, a correlation matrix at the present was created to establish the directionality of associations between attitude toward aging/preparing behavior for old age and demographic/clinical variables. Stepwise multiple regressions were then used to examine determinants at the present or predictors in the past for both the attitude toward aging and the preparing behavior. The demographic/clinical variables entered into the equations as independent variables were as follows: age; length of hospital stay; positive symptom, negative symptom and general psychopathology subscales of PANSS; MMSE score; GAF score;

REHAB general behavior subscale; SFS total score; and WHOQOL26 average score. Analyses were two-tailed with the significance level set at 0.05.

RESULTS

The mean score on the Preparing Behavior for Old Age Scale was 9.35 (SD = 2.02) and that on the Attitude toward Aging Scale was 5.12 (SD = 2.61). Cronbach's coefficient alpha of the Preparing Behavior for Old Age Scale was 0.611 and that of the Attitude toward Aging Scale was 0.693.

Table 1 shows that the mean age was 56.7 years at the time of the past evaluation. The mean number of days of hospitalization was 9061.0 (24.8 years) at the time of the past evaluation and 9090.0 at the time of the present evaluation (after discharge, some of the patients with schizophrenia briefly entered a hospital once again).

As shown in Table 2, testing of the correlations between attitude toward aging/preparing behavior for old age at the time of the present evaluation and various factors revealed that the Preparing Behavior for Old Age Score was significantly correlated with the lengths of the hospital stay (negative correlation, $r = -0.326$, $P < 0.05$) and the WHOQOL26 average score (negative correlation, $r = -0.518$, $P < 0.001$), while the Attitude toward Aging Score was significantly correlated with the WHOQOL26 average score (positive correlation, $r = 0.377$, $P < 0.05$).

A stepwise multiple regression analysis using demographic/clinical variables as determinants was generated for both the attitude toward aging and the preparing behavior for old age to identify determinant variables most closely associated with the outcome variables at the present. Table 3 shows that the model for the preparing behavior for old age using variables obtained at the time of the present evaluation was significant and included only the WHOQOL26 average score as a determinant. This means that a higher QOL was related to less active preparing behavior for old age. The model for the attitude toward aging using variables obtained at the time of the present evaluation was also significant and included the WHOQOL26 average score. This means that a higher QOL was related to a more positive attitude toward aging at the time of the present evaluation.

Table 2 shows that testing of the correlations between attitude toward aging/preparing behavior for old age at the time of the past evaluation and

Table 1. Changes in demographic/clinical variables after transition from residential care to community dwelling ($n = 57$)

	Present (community-dwelling)		Past (residential care)	
	Mean	SD	Mean	SD
Age (years)	56.7	6.9	59.7	6.9
Length of hospital stay (days)	9090.0	3576.1	9061.0	3560.3
MMSE	25.1	3.7	26.6	3.3
PANSS (P)	8.8	3.1	8.7	2.7
PANSS (N)	13.9	5.2	14.3	5.5
PANSS (G)	22.5	5.5	22.4	5.2
GAF	64.8	12.8	66.6	12.3
REHAB	42.2	28.0	41.3	22.4
SFS	106.9	28.5	112.4	19.4
WHOQOL26	3.28	0.40	3.15	0.43

GAF, Global Assessment for Functioning; MMSE, Mini-Mental State Examination; PANSS, Positive and Negative Syndrome Scales: (P) Positive symptom, (N) Negative symptom, (G) General psychopathology; REHAB, Rehabilitation Evaluation Hall and Baker scale; SFS, Social Functioning Scale; WHOQOL26, 26-item short form of the World Health Organization Quality of Life scale.

various factors revealed that the Preparing Behavior for Old Age Score was significantly correlated with the lengths of the hospital stay (negative correlation, $r = -0.327$, $P < 0.05$) and the WHOQOL26 average score (negative correlation, $r = -0.315$, $P < 0.05$).

Table 3 shows that a stepwise multiple regression analysis using data on the preparing behavior obtained at the time of the past evaluation was significant and contained two variables: the WHOQOL26 score and the length of hospitalization. These

Table 2. Pearson coefficients for correlations between preparing behavior for old age/attitude toward aging and demographic/clinical variables at the times of the present and the past evaluations ($n = 57$)

	Present		Past	
	Preparing behavior for old age	Attitude toward aging	Preparing behavior for old age	Attitude toward aging
Age	-0.106	-0.133	-0.106	-0.133
Lengths of hospital stay	-0.326*	-0.068	-0.327*	-0.067
MMSE	0.125	-0.178	0.129	-0.144
PANSS (P)	-0.096	0.177	-0.004	0.161
PANSS (N)	0.091	0.083	0.183	0.018
PANSS (G)	-0.079	0.198	0.012	0.163
GAF	-0.043	-0.167	0.008	-0.251
REHAB	0.080	0.175	-0.015	0.123
SFS	-0.209	0.187	-0.093	0.161
WHOQOL26	-0.518**	0.377*	-0.315*	0.132

* $P < 0.05$. ** $P < 0.001$.

GAF, Global Assessment for Functioning; MMSE, Mini-Mental State Examination; PANSS, Positive and Negative Syndrome Scales: (P) Positive symptom, (N) Negative symptom, (G) General psychopathology; REHAB, Rehabilitation Evaluation Hall and Baker scale; SFS, Social Functioning Scale; WHOQOL26, 26-item short form of the World Health Organization Quality of Life scale.

Table 3. Stepwise multiple regression models for attitude toward aging/preparing behavior for old age with demographic/clinical variables at the time of the present evaluation as determinants and at the time of the past evaluation as predictors

	Dependent variable	Independent variables	Beta	P-value	
Present	Preparing behavior for old age	WHOQOL26	-0.505	<0.001	($F = 18.457$; $df = 1, 56$; $P < 0.001$; $R^2 = 0.241$)
	Attitude toward aging	WHOQOL26	0.319	0.016	($F = 6.138$; $df = 1, 56$; $P = 0.016$; $R^2 = 0.085$)
Past	Preparing behavior for old age	WHOQOL26	-0.314	0.016	($F = 6.697$, $df = 2, 55$;
		Lengths of hospital stay	-0.324	0.013	$P = 0.003$; $R^2 = 0.180$)
	Attitude toward aging	NA	-	-	-

NA, not applicable; WHOQOL26, 26-item short form of the World Health Organization Quality of Life scale.

results mean that a longer hospitalized period at the time of the past evaluation was related to less active preparing behavior, and a higher QOL at the time of the past evaluation was related to less active preparing behavior. No model for attitude toward aging was significant.

DISCUSSION

The determinants at the present evaluation (community-dwelling) and the predictors at the past evaluation (residential care) were detected using multiple regression analyses. The QOL related to both the attitude toward aging and the preparing behavior at the time of the present evaluation: a higher QOL was related to a more positive attitude toward aging and less active preparing behavior. The predictors of preparing behavior for old age were QOL and the length of the hospital stay: a longer hospitalized period and a higher QOL predicted less active preparing behavior.

Hiraoka¹⁷ studied healthy individuals aged 60 years or older using the Preparing Behavior for Old Age Scale. The scores for family relationship and economy were lower in our study, although the total score was comparable with that of the previous study. Usami¹⁶ examined middle-aged nurses using the Attitude toward Aging Scale. The scores for the medical and welfare preparedness, and intergenerational relationships in our study were clearly higher than those of the study by Usami. Thus, the features of preparing behavior and attitude toward aging in individuals with schizophrenia dwelling in the community seemed to differ from those of healthy individuals.

This study revealed a correlation between preparing behavior for old age and QOL in patients with

schizophrenia: the higher the QOL, the less active the preparing behavior. This result was in contrast to the result obtained for healthy individuals. In a study of healthy individuals aged 35–64 years, significant associations between preparing behavior and life satisfaction, interpersonal relationships and social participation were observed, and no significant association between preparing behavior and age was seen.²⁸

If healthy individuals are satisfied with their life, they behave with their future life in mind if they have a sufficient economic margin.¹⁷ In contrast, individuals with schizophrenia did not behave with the future in mind even if they were satisfied with their life. Our study clearly indicated higher attitude-toward-aging scores in the category of medical and welfare preparedness, interpersonal relationships and independent life compared with the results of the study by Usami.¹⁶ In other words, community-dwelling individuals with schizophrenia seemed to have a positive perspective on medicine, welfare and economy. In addition, the scores for category of family relationship and economy for the Preparing Behavior for Old Age Scale were lower in our study than in the study by Hiraoka.¹⁷ As welfare guarantees a minimum livelihood, the patients may not need to make an effort to prepare for their future lives.

On the other hand, general cognitive function assessed using the MMSE was not associated with preparing behavior in our study. Generally speaking, it is not surprising that schizophrenia patients with good cognitive function (that is, they have sufficient self-monitoring with regard to their life) can recognize difficulties with their current lives and may want to make an effort to provide for their future. Although the correlation between cognitive function, especially frontal lobe function, and QOL has been