

Systematic Review of Accelerated Biological Aging in People with a Serious Mental Illness

Introduction

5.5% of the population of the United States has a serious mental illness (SMI)¹ with a per-patient burden of 1.85 million dollars.^{1,2} SMI is defined as schizophrenia, schizoaffective disorder, bipolar disorder, or treatment-refractory major depressive disorder.³ SMI can strain the body and may impact biomarkers associated with accelerated aging. Accelerated aging is defined as an individual's biological age exceeding a person's chronological age.⁴ Given the growing evidence that psychosocial interventions may impact biological aging in individuals with SMI, these findings may suggest that psychosocial interventions are associated with life prolongation and represent a potential strategy to increase the lifespan of people with SMI.

Objective

The purpose of this presentation is to outline the findings of a systematic review on studies that measure biomarkers of accelerated aging in individuals with serious mental illness while investigating a psychosocial intervention.

Methodology + Analysis

According to the PRISMA guidelines, the participants, interventions, comparisons, and outcomes (PICO) criteria were used to assess study eligibility in partnership with a librarian. We included studies that focused on the general population with psychosocial intervention, no psychosocial intervention as a comparison, and outcomes of early death. We searched the following databases from 1946 to January 2024: Medline, PsycINFO, Cochrane Central Register of Controlled Trials, Scopus, and PubMed. The search of Scopus returned 2651 results; PsycINFO, 651 results; Medline, 950 results; and Cochrane Library, 1426 results. Of these studies, our inclusion criteria yielded 3971 results with duplicates removed. After limiting the criteria to serious mental illness instead of mental health disorders agnostic, 52 studies were left available. From these studies, 32 RCTs were considered to fit the criteria. The removed ones were either not RCTs, needed the proper age criteria or more data, were duplicates, or needed to be completed studies. Methodological Quality Rating Scale (MQRS) was used to assess the methodological quality of included studies.

Key Definitions

Psychosocial Intervention: interpersonal or informational activities, techniques, or strategies that target biological, behavioral, cognitive, emotional, interpersonal, social, or environmental factors with the aim of improving health functioning and well-being.
Biomarker: indicators signaling events in biological systems or samples and as tools to clarify the relationship between exposure and health impairment.
Serious Mental Illness: schizophrenia, schizoaffective disorder, bipolar disorder, or treatment-refractory major depressive disorder.

Results/Findings

The majority of participants were male (62.2%). For the 14 studies that reported on race, 66.34% of participants were white, 35.3% were black, 8% were Hispanic, 2.6% were Aboriginal or Torres Strait Islander, 84% were Australian, 4.5% were Asian, 0.4% were native Hawaiian, and 9.0% were other in studies that reported on that particular racial or ethnic category. Age averaged 40.78 years for all 28 studies that reported age. The highest average age in a study was 55, and 24 was the lowest average age in a study.

The MQRS scores ranged from 6 to 15, (M = 11.26, SD = 2.05) and a median score of 11; three studies had a score over 14, indicating a high-quality study. Factors that contributed to lower scores included lack of collaterals, (N = 34, 100%) and the follow-up being non-blind or unspecified (N = 30, 88.24%) Strengths included the dosage treatment being enumerated and accounted (N = 33, 97.1%), provision of sufficient information for replication (N = 33, 97.1%), and inclusion of baseline characteristics (N = 34, 100%).

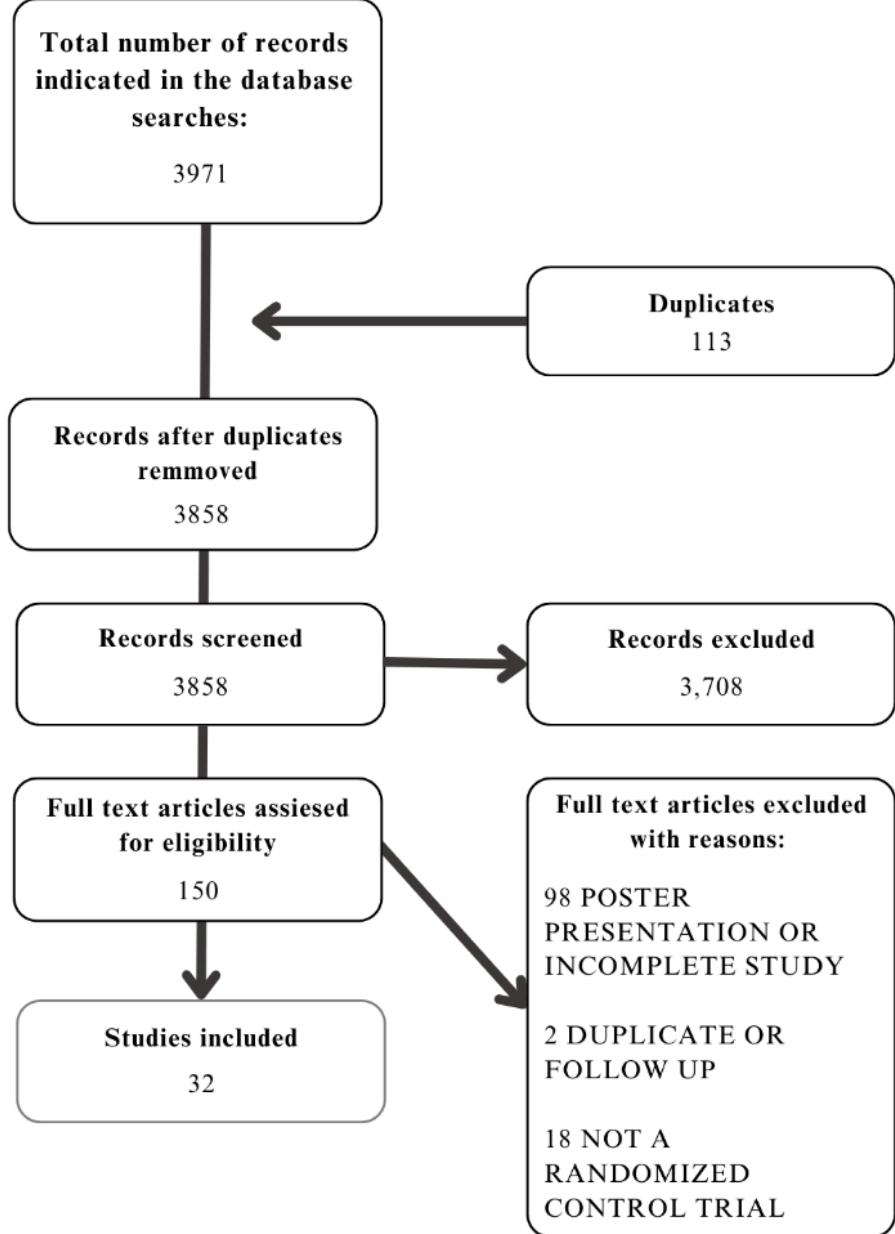
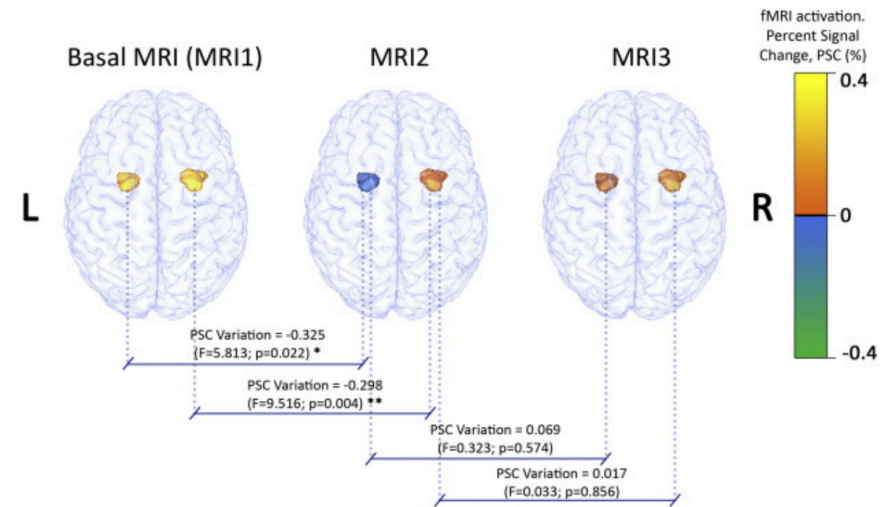
Studies assessed biomarkers, which were grouped into four categories.

Brain-based biomarkers included brain-derived neurotrophic factor (BDNF), pituitary volume, mismatch negativity pMMN, electrophysiology, matrix metalloproteinase-9 (MMP-9), functional magnetic resonance imaging (fMRI), and neuropeptide S (NPS).

Behavioral biomarkers including digit span, perseverative error, category achievement, ethyl glucuronide, other substance use, pupillometry, facial affect matching task, Framingham risk assessment, cardiorespiratory fitness, sedentary time, physical activity (walking time and daily exercise included), and energy intake.

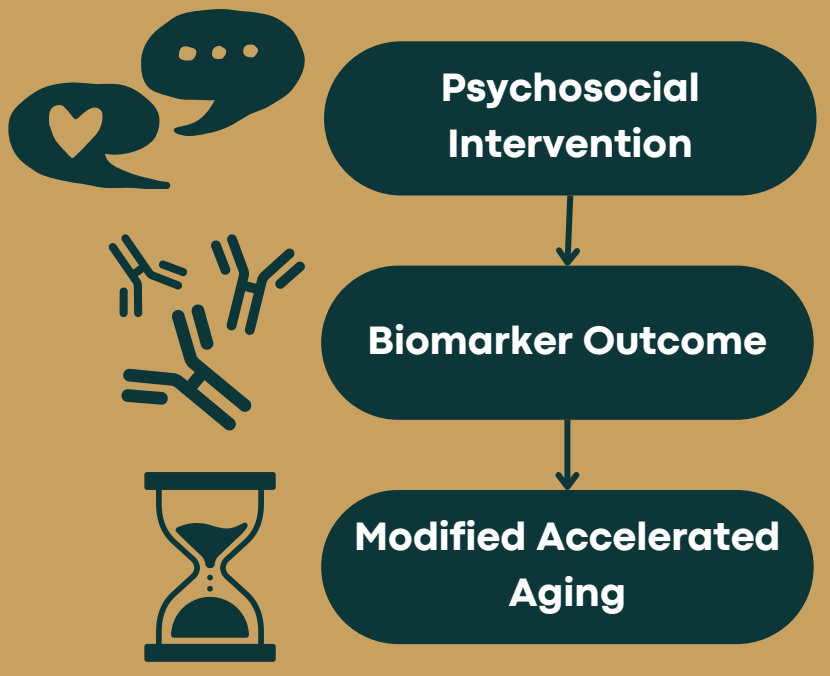
Immune biomarkers included granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-5 (IL-5), interleukin-12 (IL-12), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), soluble tumor necrosis factor receptor 2 (sTNF-R2), C-reactive protein, and cortisol.

Metabolic biomarkers included cardiovascular risk factors, body mass index (BMI), waist circumference, blood pressure, cholesterol, insulin, glycosylated hemoglobin (HbA1c), blood glucose, weight, triglycerides, resting heart rate, forced expiratory volume, and salivary amylase. Immune biomarkers were the least recorded among the studies but were positively correlated with changes in the psychosocial intervention treatment group. Metabolic biomarkers were the most studied, and brain-based and behavioral biomarkers were heterogeneous.



Conclusion

Psychosocial interventions are relatively effective and affordable for treating SMI, and the objective precision of biomarkers correlates to accelerated aging. Therefore, we suggest that psychosocial intervention randomized control trials with biometric outcomes may represent a viable strategy for reducing disease burden and improving human health. Additional research is needed to elucidate the mechanisms through which psychosocial interventions exert relatively long-lasting, beneficial effects on biomarkers of accelerated aging and serious mental illness. The present systematic review extends this work by identifying the types of biomarkers strongly associated with psychosocial intervention and accelerated aging, the biomarkers outcomes consistently associated with these interventions, and the various factors that could moderate these associations.



Methodological Attributes	Points Assessed
A. Study design:	1 = Single group pretest posttest. 2 = Quasi-experimental (nonequivalent control). 3 = Randomization with control group.
B. Replicability:	0 = Procedures contain insufficient detail. 1 = Procedures contain sufficient detail.
C. Baseline:	0 = No baseline scores, characteristics, or measures reported. 1 = Baseline scores, characteristics, or measures reported.
D. Quality control:	0 = No standardization specified. 1 = Intervention standardization by manual, procedures, specific training, etc.
E. Follow-up length:	0 = Less than 6 months. 1 = 6 to 11 months. 2 = 12 months or longer.
F. Dosage:	0 = No discussion of dosage or % of treatment received. 1 = Dosage, % treatment enumerated and accounted for.
G. Collaterals:	0 = No collateral verification. 1 = Collaterals interviewed.
H. Objective verification:	0 = No objective verification. 1 = Verification of records (paper records, blood, materials, etc.).
I. Dropouts / attrition:	0 = Dropouts neither discussed nor accounted for. 1 = Dropouts enumerated and discussed.
J. Statistical power:	0 = Inadequate power due to sample size/dropouts. 1 = Adequate power with adequate sample size.
K. Independent:	0 = Follow-up nonblind, unspecified. 1 = Follow-up of interventions treatment-blind.
L. Analyses:	0 = No statistical analyses or clearly inappropriate analyses. 1 = Appropriate statistical analyses (group differences, characteristics comparable).
M. Multisite:	0 = Single site or comparison of differing intervention. 1 = Parallel replications at two or more sites.

NOTE: Adapted from Miller et al. (1995). Scores could range from 0 (low)

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