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PRIMARY PSYCHOSIS, GERIATRIC DEPRESSION AND COGNITIVE RESERVE: PROTECTIVE FACTOR AND THERAPEUTIC TRAJECTORS

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SUMMARY

Cognitive reserve (CR) is essential in reducing natural cognitive decline. Identified in neurodegenerative pathologies, it also increasingly plays a role in the development of the symptomatic processes of numerous psychiatric pathologies. CR could help identify subgroups of elderly patients affected by primary psychosis and mood disorders and evaluate their correlation with diagnostic and therapeutic trajectories. Our observational study assessed the correlation between cognitive reserve and cognitive and psychopathological trajectories in a group of elderly inpatients in health residential centers. After two years of observation, the results indicate a correlation between cognitive reserve levels and psychopathological and cognitive trajectories. No significant variations or correlations were observed between another investigation factor, aberrant salience, and the symptoms in the above trajectories.

Key words: *cognitive reserve - aberrant salience - primary psychosis - mood disorders - cognitive domains - early symptoms*

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INTRODUCTION

One of the emerging debates in recent scientific literature concerns the importance, methods, and necessity of prevention in the psychological and psychiatric fields (Adrien et al. 2023). The complexity of intercepting the first symptoms of future psychiatric pathologies raises several educational and clinical questions. The complex and multi-dynamic universe of prepsychotic personalities or temperaments has always posed enormous diagnostic and therapeutic problems (Franza & Tavormina 2022). Furthermore, discoveries in the neuroscientific field increasingly highlight the importance of early biochemical and structural alterations, which will determine the explosion of relevant psychopathological symptoms at a later age (Rogantini et al. 2022). Early identification and diagnosis would make it possible to avoid or reduce the severity of the onset of these pathologies. Leaving aside the large literature on the subject and returning to the most recent discoveries of neuroscience, it is necessary to underline some decisive steps in the study of these topics (e.g., the discoveries of mirror neurons, the pruning phenomenon, the role of the connection in the genesis of psychiatric disorders) (Georgiadis et al. 2024, Bonini et al. 2022). Several factors can influence the future psychopathological and therapeutic trajectories of psychiatric disorders. Studies on cognitive reserve (CR) and aberrant salience (AS) are beginning to emerge. The cognitive reserve can be described as the brain's ability to find alternative ways to try to complete a job, task, and/or activity as best as possible (Stern et al. 2020). Assuming the overall involvement of the cognitive domains in the clinical course of these pathologies, attention can be directed to the quantification of cognitive deficits and their deterioration or worsening in specific diagnostic groups (Franza 2022).

A greater cognitive reserve in patients affected by psychiatric disorders could favor prognostic trajectories in terms of the temporality of the therapeutic intervention of the multidisciplinary team, improve the services provided and reduce the times and costs of interventions. Therefore, it is evident that among the factors that can influence the outcome and dynamic trajectories of these psychiatric pathologies, the study of the cognitive domains of each individual and the so-called cognitive reserve can be fundamental. (Sheffield et al. 2108, Tsitsipa & Fountoulakis 2015, Fusar-Poli et al. 2013).

Instead, the pervasive experience of aberrant salience could be an initial index for the evaluation over time of the psychopathological evolution of pathologies in patients with subthreshold symptoms.

Our multicenter study aimed to evaluate the role of cognitive reserve and aberrant salience in guiding symptomatic and therapeutic trajectories in elderly patients suffering from mood disorders and primary psychosis.

METHOD

Our observational study was conducted using an "exploratory design" to understand and identify a particular phenomenon. The patients were affected by psychiatric disorders classified according to the DSM-5 diagnostic criteria. Eighty-seven patients (age ≥ 65 years) affected by bipolar disorder (BD) type I and type II, major depressive disorder (MDD), and schizophrenia (S) were selected in three residential health centers located in Southern Italy (Psychiatric Rehabilitation Centre "Villa dei Pini, Avellino, Italy, Social Cooperative Centre "Il Filo di Arianna, Venosa (PZ), Italy; RASS1 (Social-Health Residence for the Elderly) "Villa Caterina", Pescopagano (PZ), Italy. Patients with severe organic pathologies (metabolic syndrome, severe cardiovascular diseases, and neuro-degenerative disorders) were excluded from the study. After collecting the authorizations and informed consent according to the reception protocols in any center, the staff involved in the study were guided by the coordinators of each facility involved in administering the evaluation material. The following data were collected for each patient: age, sex, marital status, education, and years of working activity. These variables were collected directly from the caregiver interview and reported on a spreadsheet for subsequent statistical evaluation. These parameters were collected at the beginning of the study period (T0).

All patients were administered the following evaluation scales:

- *Aberrant Salience Inventory (ASI)* (Cicero et al. 2010): for evaluating aberrant salience.
- *Cognitive Reserve Index questionnaire (CRIq)* (Nucci et al. 2012): for evaluating cognitive reserve.
- *Brief Psychiatric Research Symptoms (BPRS)* (Overall & Gorham 1988): for psychopathological evaluation.
- *Epitrack* (Lutz & Helmstaedter 2005): to evaluate the following cognitive domains: response inhibition, visuomotor speed, mental flexibility, visuomotor anticipation, rapid lexical access, working memory.

The first rating scales (ASI and CRIq) were administered only at the baseline (T0) to evaluate the initial AS and CR scores from which to assess symptom trajectories in T1 (after 6 months), T2 (after one year), and T3 (after 2 years) with other rating scales (BPRS, and Epitrack).

The quantitative data we collected into Microsoft Excel spreadsheets, a platform known for its reliability and standardization. For single independent sample data in T0, Cronbach's alpha, α was evaluated. A significance level of $p \leq 0.05$ was considered statistically significant, ensuring the robustness of our findings.

EZAnalyze 3.1 is a free Microsoft Excel Add-In designed to enhance Excel's capabilities by adding "point and click" functionality for data analysis, charting, and creating new variables.

RESULTS

The data obtained indicate significantly adequate age, gender and education levels in the CRQi scale. The two-factor analysis of variance without replication for an independent sample revealed one factor (Cronbach's alpha), with acceptable reliability [α=0.8757 (T0) P-value: 0.007; F Crit: 0.325]. This overall value in two groups of patients analyzed (BD I, II, and MDD) showed overlapping reliability levels in both groups [BD vs MDD respectively (mean =50.27 vs 47.68; Stat t 0.97, P (T<=t) one tail 0.167; t critical one tail 1.663). In the group of patients with schizophrenia, Cronbach's alpha presented acceptable reliability of a moderate degree [α=0.4567 (T0) P-value: 0,1012; F Crit: 1.264]. These results indicated a sufficient criterion of statistical reliability for analyzing cognitive and psychopathological trajectories.

Evaluating the results obtained with the ASI in the sample groups analyzed indicates adequate reliability values (Cronbach's alpha α=0.776 (T0); P-value: 0.008; F crit: 1.481]. Also, in this case, the data are reliable and comparable in the three groups of patients analyzed (BD I, II, MDD, and S) (Figure 1, 2).

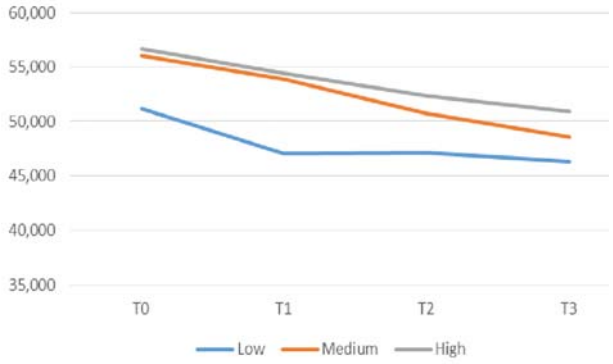

Figure 1. ASI vs BPRS – Mood Disorders

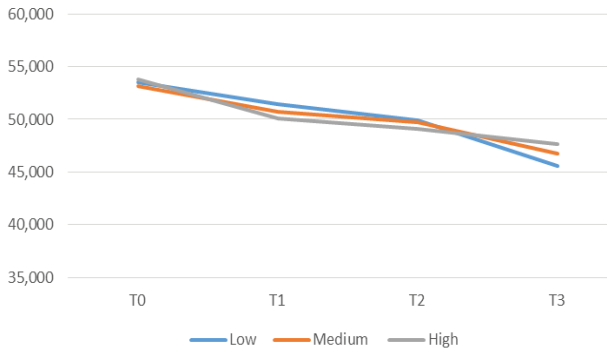

Figure 2. ASI vs BPRS – Schizophrenia

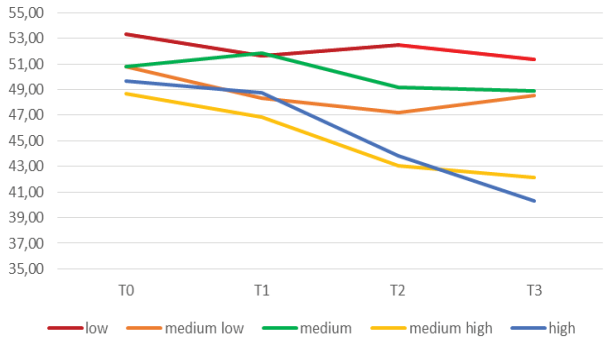

Figure 3. CRIq vs BPRS

The data obtained with the BPRS highlighted a statistically significant variation in the average scores at each evaluation time. The results obtained with ANOVA Repeated Measures indicate that at least two of the repeated measures differ quantitatively [P 0.0000; Eta Squared 0.163 (Figure 3). The differences in the means between T1 and T3 are particularly significant (P – Bonferroni = 0.005) and between T0 e T3 (P - Bonferroni = 0.000).

The data obtained with CRQi and the symptomatological changes of patients evaluated with BPRI were compared. The groups of low, medium-low, medium, medium-high, and high scores of the study participants were considered. The graph highlights the correlation between CRQi and BRPR at the different times analysed. The data reveal a close correlation between high CRQi levels and a reduction, although not statistically significant, in BPRS scores. Importantly, no significant correlations were found between the levels of scores obtained with the ASI and the evolution of the average BPRS scores, indicating a distinct lack of relationship between these variables.

The data obtained with Epitrack confirm previous studies which indicated a statistically significant reduction in total scores in the groups analysed, with a particular impact on the visomotor speed and working memory domains. The ANOVA results indicate that at least two repeated measures differ significantly. Specifically, T0 vs T3 (P - Unadjusted 0.019; P - Bonferroni 0.035) and T0 vs T3 (P - Unadjusted 0.011; P - Bonferroni 0.114).

DISCUSSION

The evaluation of cognitive reserve in the groups analyzed indicated higher baseline scores associated with quantitatively less significant cognitive deficits in patients affected by primary psychosis. These data are consistent with other studies carried out on the cognitive domains of patients suffering from psychiatric disorders (Franza et al. 2018). Working memory, inhibition, and flexibility have been most strongly associated with cognitive reserve (Cotrena et al. 2021). The cognitive reserve can positively influence all cognitive domains analyzed in our study. In a recent review, Matsumoto and Hamatani (2024) observed that people with high cognitive reserve may have fewer bipolar episodes and a reduction in cognitive disorders and dysfunctions.

Furthermore, cognitive reserve can maintain the functional level in patients with bipolar disorder. Indexed by a composite score based on multiple indicators, it may moderate the negative association between reduced mood and cognitive impairment, underscoring the importance of continuing to build CR throughout life to maintain cognitive health (Opdebeeck et al. 2018). People with bipolar disorder have more significant cognitive difficulties that tend to be more pronounced during mood episodes but persist after clinical remission and affect recovery. Recent evidence suggests heterogeneity in these difficulties, but the factors underlying cognitive heterogeneity are unclear. Individuals with cognitively impaired profiles demonstrate more significant cognitive decline after disease onset. Cognitive reserve may be one of the factors underlying cognitive variability in people with bipolar disorder. Patients in the intermediate and severe subgroups may need interventions targeting cognitive difficulties (Tsapekos et al. 2020). The problems and difficulties of a correlation between cognitive reserve and aberrant salience are more pronounced in these disorders, and the results obtained from our study require a complex analysis. It is believed, however, from the first observations that detecting the correlation was impossible. Statistical insights are therefore postponed to subsequent evaluations.

CONCLUSION

The findings from our study are preliminary and raise several important issues. However, they suggest that cognitive reserve may play a protective role in the overall functioning of individuals with mood disorders. Higher levels of aberrant salience do not impact this patient group significantly. Cognitive reserve might help predict the diagnostic and treatment paths for patients with mood disorders. It could serve as a valuable indicator for identifying specific subgroups of patients who would benefit from tailored cognitive rehabilitation activities. Customized rehabilitation programs targeting specific cognitive areas could help slow natural cognitive decline. This approach could lead to improvements in various cognitive functions and have a direct impact on the symptomatic progression of mood disorders and psychotic disorders.

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Conflict of interest: *None to declare.*

Contribution of individual authors:

Francesco Franza: design of the study, statistical design, interpretation of the data & writing manuscript.

Barbara Solomita: sample collecting, literature research, first draft, writing manuscript.

Andreana Franza: sample collecting, literature research, writing and translation manuscript.

Giuseppina Conte, Maria Vincenza Minò, Lucrezia Roselli & Antonella Vacca: sample collecting, literature search, interpretation data.

Giuseppe Tavormina: supervision, interpretation of the data, approval of the final version.

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