Cognitive impairment in patients with psoriasis: A matched case-control study

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ABSTRACT

Background: In the past decade, a few studies have suggested that psoriasis could be associated with the presence of mild cognitive deficits.

Objectives: The aim of the present matched case-control study was to investigate several cognitive domains (executive functions, verbal memory, attention, and language) in a sample of outpatients with psoriasis. We also investigated whether cognitive impairment was associated with poor health-related quality of life (HRQoL) in patients with psoriasis.

Methods: Fifty adult outpatients and 50 age- and sex-matched healthy controls were administered a battery of neuropsychological tests investigating major cognitive domains, psychopathology (anxiety and depression), alexithymia, and HRQoL.

Results: At the bivariate level, psoriasis patients (compared to healthy controls) performed worse on most of the neuropsychological tests, and they also reported more anxiety and depressive symptoms, higher scores for alexithymia, and worse physical and mental health. At the multivariate level, cognitive performance was independently associated with psoriasis even when controlling for psychopathology and alexithymia.

Conclusions: Patients with psoriasis show impaired cognitive performance, high levels of anxiety and depression, and impaired quality of life. Based on the current results, clinicians should assess the presence of psychological symptoms in their patients and evaluate whether the presence of cognitive deficits is limiting the patients' ability to cope with the disease.

1. Introduction

Psoriasis is a common chronic inflammatory skin disease with psychiatric and medical comorbidity (e.g., obesity, diabetes mellitus, and depression) [1,2]. Prevalence estimates for psoriasis range from 1.4% to 3.3% with wide geographical and ethnic differences [3]. Psoriasis causes considerable disability and affects the quality of life of patients [4–8].

Psychological factors play an essential role in the etiology and prognosis of psoriasis, and also in the management of the illness [9]. Psychiatric disorders, notably anxiety and depression, are common comorbidities in psoriasis [10–13]. For example, in the US population, Cohen et al. [14] found that 16.5% of patients with psoriasis met the criteria for major depression. Psychological conditions have been generally considered as responses to the stress of living with a chronic and disabling condition that also comes with social stigma. Nevertheless,

some researchers, building on the so-called "*Brain-skin axis*" hypothesis [15], have begun to study neurocognition in patients with psoriasis [16–20]. This research has suggested the possible presence of mild cognitive impairment in up to 44% of patients with psoriasis [18]. For example, Colgecen and colleagues [16] found deterioration of the cognitive performance of patients with psoriasis, especially in visual-spatial and executive tasks, but no correlations with disease characteristics (e.g., duration, severity, and onset age). Gisondi et al. [18] also reported reduction in cortical thickness in parahippocampal, superior temporal and frontal gyri of the left hemisphere.

However, to date, only a small number of studies, frequently using small samples, single screening instruments [16], and noncontrolled cross-sectional designs, have supported these results [17]. Thus, the objective of the present matched case-control study was to extend results from previous studies by investigating several cognitive domains (executive functions, memory, attention, and language) in a sample of

outpatients with psoriasis. We also investigated whether cognitive impairment was associated with decreased health-related quality of life (HRQoL) in patients with psoriasis. Based on previous research, we hypothesized that: (1) patients with psoriasis are more likely to have deficits in most of the cognitive domains investigated when compared with sex- and age-matched healthy controls, even after controlling for the severity of anxiety, depression and alexithymia; (2) cognitive impairment is associated with decreased HRQoL; and (3) cognitive impairment severity is not correlated with clinical variables (i.e., severity of the illness and onset age, even when controlling for socio-demographic characteristics).

2. Material and methods

2.1. Sample

Fifty adult outpatients (22 women and 28 men) consecutively admitted at the Center for the Study and Treatment of Psoriasis of the San Gallicano Hospital (Rome, Italy) between November 2016 and May 2017 participated in a matched-case control study. Inclusion criteria were age between 18 and 60 years old and a diagnosis of psoriasis vulgaris with a Psoriasis Area Severity Index (PASI) > 3 [21]. Exclusion criteria were the presence of major diseases of the central nervous system (e.g., dementia and Parkinson disease) and a history of head injuries or strokes; the presence of specific medical conditions, such as hypertension, diabetes mellitus, and dyslipidemia, or other immune-mediated diseases sharing the same physiological mechanism as psoriasis (e.g., Crohn's disease, psoriatic arthritis, and rheumatoid arthritis), and current major psychiatric disorders (e.g., schizophrenia and bipolar disorder) or hallucinatory and delusional phenomena; and the inability to complete the assessment for whatever reasons, including denial of informed consent.

Each patient was matched for sex and age with a healthy control (22 women and 28 men). The controls were recruited from those attending adult education classes and from an advertisement posted for established community groups. The same inclusion/exclusion criteria used for the patients were used for the controls. Furthermore, we excluded possible controls with current or past diagnosis of psoriasis and people with a positive history of psoriasis in their family members. The sociodemographic and clinical characteristics of the sample are reported in Table 1. The protocol received approval from the local Institutional Review Board.

2.2. Measures

All participants were administered a checklist assessing socio-demographic variables (sex, age, marital status, job, school attainment, and hand laterality) and a battery of neuropsychological tests. Tobacco, alcohol and drug use were assessed with one item each of the checklist. Participants were asked whether they were currently smoking tobacco (and how many cigarettes they were smoking daily), drinking alcohol beverages (and how frequently they drink during the week), and using illegal or nonprescribed drugs (including legal highs, and how frequently they used drugs during the week). Neuropsychological tests were administered in a single session and in a fixed order. For the patient sample, clinical information (years with the illness, comorbidities, family history of psoriasis) were retrieved from clinical records, and the PASI was completed by the dermatologist in charge 7–14 day before administering the tests. The PASI (score range: 0–72) assesses four body regions (head, trunk and upper and lower extremities) for the body surface area involvement of erythema, infiltration, and desquamation [21].

2.3. Neuropsychological assessment

2.3.1. Cognitive functioning

The Mini Mental State Examination (MMSE) is a widely used and well-validated screening tool for cognitive impairment [22,23]. The items of the MMSE include tests of orientation, attention, learning, calculation, abstraction, information, construction, and delayed recall. Sum scores range between 0 and 30, with lower scores indicating the possible presence of cognitive impairment. The diagnostic accuracy and clinical utility of the MMSE in screening for dementia have been reported [23,24].

The Rey Auditory Verbal-Learning Test (AVLT) [25,26] was used to evaluate verbal memory. In the present version of the AVLT, a 15 noun-word list was read five times to the participants with a presentation rate of one word per second, and after each trial the participant was immediately asked to recall as many words as possible (AVLT-I). After a 20 min delay, the participant was again asked to recall the words from the list (AVLT-D). The numbers of correct words (range of scores 0–75 points for the AVLT-I and 0–15 for the AVLT-D) and intrusions were recorded. We used age- and education-corrected scores [27]. The AVLT has demonstrated good ability to screen for mild cognitive impairment [28], and good predictive validity for Alzheimer's dementia type [29].

The Trail Making Test (TMT) [30–32] is widely used as a measure of organized visual search, planning, attention, set shifting, cognitive flexibility, and divided attention. The test consists of two parts. In part A (TMT-A), participants are asked to draw a line joining a series of high contrast dots which are numbered from 1 to 25. In part B (TMT-B), participants are asked to join a series of numbers and letters in an alternated sequence. A participant's score was taken as the time to complete the test. The TMT is a reliable measure when testing executive functioning [32], with good ability to screen for Alzheimer's dementia type [33].

The Attentive Matrices Test [34] is a measure of selective and sustained attention, with good ability to screen for Alzheimer's dementia type [35]. The participant is required to find target numbers (from one to three) in 3 numeric matrices (10 columns of 13 numbers from 0 to 9). A participant's score is the number of targets correctly found and the numbers of false alarms and omissions. We used sex-, age-, and education-corrected scores [34].

The Forward and Backward Digit Span test [36,37] measures the longest digit span recalled in both forward and backward recall. Forward recall assesses auditory attention and short-term retention capacity; backward recall measures the ability to manipulate information in verbal working memory. The Backward Digit Span has been reported to have good ability to screen for Alzheimer's dementia type [38]. We used age- and education-corrected scores [39].

The Clock Drawing Test (Clock Test) [31,40] is a visuospatial task capable of assessing several abilities including visuoconstructive abilities, and executive and praxic functions. We presented a pre-drawn circle in which the participants were instructed to draw in the numbers and then set the time at 2:45 pm. The scoring procedure evaluates quantity and positioning of numbers and hands (scores range 0–10) [31]. The Clock Test can reliably screen for cognitive impairment in clinical settings [41].

The Phonemic Fluency Test (Fluency Test) [31] measures verbal ability and executive control [31,42,43]. In the Fluency Test, the participants are asked to orally produce words beginning with a given letter. The numbers of unique correct words, repetitions, and intrusions were recorded. The Fluency Test has good ability to screen for Alzheimer's dementia type [33].

The Stroop Color Word Interference Test (Stroop Test) [44,45] is a reliable measure assessing selective attention, visual attention, and inhibitory control, which has been reported being sensitive to lateral and superior medial lesions of the frontal lobes [46]. We administered a computerized version of the task, using PsychoPy, version 9. Participants were placed in front of a laptop (Lenovo® Core i5; screen 15.6″) at