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Exploratory inflammatory profiles in patients with depressive disorders and a history of cancer considering alcohol consumption

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ABSTRACT

Purpose: Psychiatric disorders, including recurrent unipolar depression and bipolar disorder, are associated with increased cancer risk and premature mortality. Alcohol use disorder (AUD) and immune dysregulation may underlie these associations.
Objectives: This exploratory study investigated whether inflammatory and neuroplasticity-related biomarkers differ according to cancer history and alcohol abstinence in patients with AUD and depressive disorders.
Methods: We conducted a retrospective analysis of 172 patients from a French clinical cohort, including 53 participants with longitudinal inflammatory and neuroplasticity biomarkers assessed over six months.
Results: Among the study sample (mean age: 45.7 years; 134 men/38 women), 12.8% had cancer history, predominantly ear, nose and throat (27.3%) and breast cancers (22.7%), with psychiatric diagnoses preceding cancer onset by approximately 15 years. IL-8 (Interleukin-8) levels were significantly higher in participants with cancer history and depressive disorders, independently of alcohol abstinence, suggesting a stable cancer-associated inflammatory signature. In contrast, TNF-α (Tumor Necrosis Factor-alpha) levels varied according to alcohol abstinence status over time, distinguishing abstinent from non-abstinent individuals independently of cancer history. BDNF (Brain-Derived Neurotrophic Factor) levels did not differ according to cancer history or abstinence.
Conclusions: These findings suggest that distinct inflammatory pathways may characterize cancer history and alcohol abstinence in patients with AUD and depressive disorders. IL-8 and TNF-α may represent candidate biomarkers associated with cancer-associated inflammation and alcohol abstinence status, respectively. Given the small cancer subgroup, these results should be interpreted as exploratory and hypothesis-generating. Future studies integrating genetic, epigenetic, and molecular markers are needed to refine these associations and support personalized approaches.

1. Introduction

Numerous contradictory data and even significant gaps exist in the field of psychiatry associated with oncology. These shortcomings notably affect the incidence of cancer among individuals suffering from specific psychiatric disorders, including recurrent unipolar depression, bipolar disorder, and schizophrenia, with a particular concentration of studies focused on the latter. Histories of depression or disorders related to alcohol or substance use have been associated with an increased risk of cancer [1], though contradictory results have been obtained for bipolar disorder [2,3]. This controversy stems from two opposing interpretations: one suggesting psychiatric disorders as independent risk factors for cancer, and another attributing observed associations to shared confounders such as lifestyle factors, alcohol use, and medical comorbidities or treatments. These confounders are particularly relevant in alcohol use disorder (AUD) and depressive disorder populations.

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Consequently, data regarding the role of mental illnesses as a risk factor for cancer remain inconclusive.

However, recent literature reports premature mortality among cancer patients with psychiatric disorders, including depression, bipolar disorder, and schizophrenia [4–6], and higher cancer mortality in patients with depression compared with non-psychiatric cancer populations [7].

Thus, the rationale for the present exploratory study is based on the observation of increased and premature mortality among patients with both psychiatric disorders and cancer. It should be noted that addiction, particularly AUD, which is highly prevalent in psychiatric populations [8], also affects cancer incidence, with 4.1% (95% CI (Confidence Interval) [3.1;5.3]) of new cases attributed to alcohol in 2020 [9]. Alcohol exposure may therefore represent a key linking factor between psychiatric disorders and cancer outcomes.

As a pioneering effort in our psychiatric institution, we have attempted to elucidate the links between specific psychiatric disorders and cancers, particularly through the temporal occurrence of each of these two pathologies as well as their associated comorbidities. This work builds on previous institutional epidemiological findings suggesting a higher prevalence of cancer in patients with recurrent unipolar depression and bipolar disorder, with frequent temporal precedence of psychiatric diagnosis over cancer onset and a high comorbidity with AUD [10]. These observations provided the clinical rationale for the present exploratory biological study.

An increase in chronic central and peripheral inflammation has been described in depressive disorders [11–14] and may contribute to increased cancer risk [15,16]. Patients with depressive disorders show elevated levels of pro-inflammatory cytokines such as IL-1β (Interleukin-1βeta), IL-6, and TNF-α (Tumor Necrosis Factor-alpha) [17]. Chronic alcohol consumption can also increase these cytokines [18] which may contribute to tumor progression, angiogenesis, and metastasis [19].

Thus, depressive disorder, AUD and cancer share common biological features related to dysregulated inflammation, which may also affect neuroplasticity pathways. Pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α can reduce BDNF (Brain-Derived Neurotrophic Factor) expression through NF-κB (nuclear factor-kappa B) and MAPK (Mitogen-activated protein kinases) signaling pathways, leading to impaired synaptic plasticity, reduced neurogenesis, and altered neuronal survival [20].

Moreover, data suggest that the rs6265 polymorphism of the BDNF gene, could be a vulnerability factor for inflammation-induced depression [21,22]. This SNP (Single Nucleotide Polymorphism) modulates gene expression, leading to reduced BDNF secretion [23], which may increase vulnerability to inflammation-associated depression and may also influence AUD severity [24] and/or relapse risk [25]. Epigenetic mechanisms may contribute to variations in BDNF expression associated with alcohol abstinence [26]. More broadly, epigenetic mechanisms have been proposed to mediate long-term effects of alcohol exposure and psychiatric disorders on inflammatory and neuroplasticity-related pathways. BDNF levels are often reduced in patients with psychiatric disorders, similarly to alcohol dependence [27] and alcohol abstinence can gradually restore BDNF levels [28]. However, the role of BDNF in the context of co-occurring depressive disorders, AUD, and cancer remains poorly understood.

This framework provided the basis for the methodological design of the present exploratory study, which aimed to investigate whether inflammatory and neuroplasticity-related biomarkers differ according to cancer history and alcohol abstinence status in patients with AUD and comorbid depressive disorders, hypothesizing that inflammatory activation is influenced by cancer history and alcohol abstinence status.

2. Methods

2.1. Preliminary institutional findings

This exploratory study is grounded in preliminary institutional findings derived from a previously described psychiatric cohort at the Esquirol Hospital Center (Limoges, France) in 2022 [10]. The original dataset included 2117 patients diagnosed with recurrent unipolar depression, bipolar disorder, or schizophrenia. Among these, patients with recurrent unipolar depression and bipolar disorder were selected, as these groups showed a higher observed prevalence of cancer diagnoses. Approximately 10% of these patients had a cancer history. In most cases (approximately 90%), psychiatric diagnoses preceded cancer onset. Breast cancer was the most frequently observed cancer type (30%). AUD was present in approximately 35% of patients with psychiatric disorders and cancer. As previously reported [10], this cohort was specifically characterized by the temporal sequencing of psychiatric disorders and cancer occurrence, cancer prevalence patterns, affected tumor sites, and alcohol consumption as a potential modifying factor in disease trajectories. These preliminary findings provided the clinical and epidemiological rationale for the present exploratory biological study.

2.2. Participants and ethics statement

Out of the 389 participants included in a previously established longitudinal cohort investigating AUD and BDNF, 172 participants were selected for the present analysis. These patients had a confirmed diagnosis of AUD established by a senior addiction specialist, and psychiatric comorbidities diagnosed by trained psychiatrists, including recurrent unipolar or bipolar depressive disorders (ICD-10 (International Classification of Diseases, 10th Revision) F33 (Recurrent depressive disorder) and F31 (Bipolar affective disorder)), based on clinical interviews and medical record review corresponding to diagnoses established at a defined clinical time point during routine psychiatric and addiction care. A cancer diagnosis was also recorded in the patients' files. Among the 172 participants, 53 patients had complete longitudinal biological data (D0 (Day 0), D28 (Day 28), M2 (Month 2), M4 (Month 4), and M6 (Month 6)) for neuroplasticity and inflammatory biomarkers reflecting the availability of stored samples and full follow-up assessments. The study received legal, administrative, and ethical approval from the French Committee for the Protection of Persons (ID-RCB: 2011-A00452-39) and the National Agency for Drug and Health Product Security (clinical trial ID: NCT01491347). All included participants provided written informed consent. The study followed the principles of the Declaration of Helsinki.

2.3. Abstinence

Abstinence was defined based on a combination of biological and clinical criteria: EtG (Ethyl glucuronide) < 1 mg/L, CDT (Carbohydrate-Deficient Transferrin) levels within laboratory reference values ($<1.7\%$ expressed as a percentage of CDT relative to total transferrin), and self-reported abstinence from alcohol with TLFB (Time Line Follow-Back). The subject was considered non-abstinent if any of these criteria were not met at each follow-up starting from that date. Total abstinence was defined as abstinence at all follow-ups during the six-month study period.

2.4. Psychometric scales

Alcohol consumption was documented using the TLFB to determine, for the two months prior to inclusion or since the last follow-up, the average number of standard drinks consumed per day, the number of days on which alcohol was consumed, and the average number of standard drinks per drinking day [29–32].

2.5. Biological analyses

2.5.1. ETG and CDT

Serum levels of CDT and urinary EtG [33,34] were measured as indicators of alcohol consumption over the previous 14 days or the last three days, respectively.

2.5.2. BDNF

Blood samples were drawn under standardized conditions and centrifuged after 1 h at 1600 xg for 5 min. The resulting serum was stored at −80 °C for later measurement. A portion of the serum was diluted 1:20, and BDNF levels were measured in duplicate on all plates to account for inter-assay variations by ELISA (Enzyme-Linked Immunosorbent Assay) following the manufacturer's instructions (R&D, Minneapolis, USA), with a standard curve as reference (62.5 to 4000 pg/mL). Optical density readings were taken at 450 nm. Intra-assay and inter-assay coefficients of variation provided by the manufacturer were below 10% for all analytes.

2.5.3. Luminex

Serum assays using the Luminex technique with the 9-Plex kit, custom-designed by Biotechne (R&D Systems), targeted the following pro-inflammatory proteins: Leptin, TNF-α, IL-1β, IFN-ɣ (Interferon-gamma), IL-6, IL-8, IL-12, IL-10, MCP-1 (Monocyte Chemoattractant Protein-1). The assays were conducted with a Luminex 100 IS flow fluorometer at the Genotoul Anexplo technology platform in Toulouse (France). Fluorescence data were analyzed with Xponent software using calibration curves from serial dilutions of protein standards. As with BDNF, samples were analyzed in duplicate. Intra-assay and inter-assay coefficients of variation provided by the manufacturer were below 10% for all analytes. This ensured acceptable analytical reliability across all inflammatory markers.

2.6. Statistical analysis

Quantitative variables are presented as mean and standard deviation. Categorical variables are described in terms of percentages and numbers. Comparisons between groups for quantitative variables were performed using the non-parametric Mann-Whitney test (cancer group and abstinence group). The Chi-squared or Fisher test (<5) was used to compare groups for categorical (nominal) variables.

Analyses over time to describe clinical evolution required a non-parametric paired Wilcoxon test when performed between two time points, preceded by a Friedman test for significant variables to assess overall differences across time points. Results with p-values <0.05 were considered significant.

Although the repeated analysis of multiple biomarkers and over different time-point analyses were performed, the increased risk of type I error cannot be excluded. No type I error correction was applied due to the small sample size, as such adjustments would be overly conservative [35]. Therefore, the present analyses should be considered as exploratory and hypothesis-generating rather than confirmatory.

The analyses were conducted using SPSS Statistics 27.0 software (IBM Corp, Armonk, NY, USA).

3. Results

3.1. General description of the sample

The sample consists of 134 men and 38 women (sex ratio: 3.53), with an average age of 45.66 ± 10.25 years. Most patients are single (102/172; 59.3%), without children (126/172; 73.3%), have a high school-level education (97/172; 56.4%), are employed for half of the group, and live on their own income (109/172; 63.4%). The majority of participants (157/172; 91.3%) had a history of alcohol withdrawal, averaging 6.13 ± 6.94 previous attempts, and consumed alcohol both frequently (5 consecutive days) (160/172; 93%) and in large quantities (5 or more drinks at a time) in the two months preceding withdrawal (168/172; 97.7%). According to the TLFB, they consumed an average of 14.81 ± 12.59 standard drinks per day over 48.51 ± 15.87 days, with an average number of standard drinks per drinking day of 17.91 ± 12.95 during the two months prior to withdrawal. The majority (153/172; 89%) were also smokers, while most did not use other substances (135/172; 78.5%). Most participants suffered from recurrent unipolar depressive disorders (112/172; 65.1%), while 60/172 (34.9%) had bipolar disorder (Table 1).

3.2. Specific description of the sample with a history of Cancer

Twenty-two participants had a history of cancer, representing 12.8% of the sample. This includes 13 men (9.7% of the male sample) and 9 women (23.7% of the female sample). Eighteen cancers were found among participants with recurrent unipolar depressive disorders, representing 15.2% of the sample, and 4 among those with bipolar disorder, accounting for 6.7% of the sample. The mean time between cancer diagnosis and study inclusion was 5.36 ± 5.55 years. Most had received

Table 1
General Description of the Sample (n = 172) at D0. (SD: Standard Deviation).

Age (years) (mean ± SD)			45.66 ± 10.25
Sex (n (%))		Men	134 (77.9)
		Women	38 (22.1)
Single (n (%))		Yes	102 (59.3)
		No	70 (40.7)
Children (n (%))		Yes	46 (26.7)
		No	126 (73.3)
Education level (n (%))		Under High School	17 (9.9)
		High School	97 (56.4)
		University	58 (33.7)
Work (n (%))		Yes	86 (50.0)
		No	86 (50.0)
Income (n (%))		Without	5 (2.9)
		Own	108 (62.8)
		Social	59 (34.3)
Withdrawal attempts history (n (%))		Yes	157 (91.3)
		No	15 (8.7)
Previous attempts number (mean ± SD)			6.13 ± 6.94
Two months prior to withdrawal	Alcohol consumption 5 consecutive days (n (%))	Yes	160 (93.0)
		No	12 (7.0)
	5 or more drinks at a time (n (%))	Yes	168 (97.7)
		No	4 (2.3)
	TLFB standard drinks per day (mean ± SD)		14.81 ± 12.59
	TLFB drinking day (mean ± SD)		48.51 ± 15.87
	TLFB number standard drinks per drinking day (mean ± SD)		17.91 ± 12.95
Smoking (n (%))		Yes	153 (89.0)
		No	19 (11.0)
Other substances comsumption (n (%))		Yes	37 (21.5)
		No	135 (78.5)
Psychiatric diagnosis (n (%))		F31	60 (34.9)
		F33	112 (65.1)
Cancer (n (%))		Yes	22 (12.8)
		No	150 (87.2)

a psychiatric diagnosis 15.50 ± 11.31 years before the onset of their cancer (20/22; 90.9%). The most common types of cancer were those affecting the ENT (Ear Nose and Throat) area (6/22; 27.3%) and breast cancer (5/22; 22.7%). Most were treated with radiotherapy, chemotherapy, and/or hormone therapy (16/22; 72.7%); others were treated with surgery alone.

When observing the subgroup with recurrent unipolar depressive disorder and a history of cancer, a significant difference favoring abstinence was noted at time M2 ($p = 0.02$). Significant differences were observed at the M2 timepoint in the subgroup with recurrent unipolar depressive disorders, which were therefore examined in subsequent analysis. These subgroup findings were not predefined but emerged from exploratory analyses, as no other timepoints or diagnostic subgroups showed notable differences.

3.3. Specific description of patients with psychiatric disorders from an inflammatory perspective: Focus on patients with a history of Cancer with or without alcohol abstinence

Among the 53 participants with biological data analyzed for their pro-inflammatory properties, there were 43 men and 10 women (sex ratio: 4.3). Most participants suffered from recurrent unipolar depressive disorders (33/53; 62.3%), while 20/53 (37.7%) had bipolar disorder. Seven participants had a history of cancer, representing 13.2% of this sample, all of whom had a psychiatric diagnosis 10.57 ± 6.11 years before the onset of their cancer. This includes 2 cases of breast cancer, 2 cases of lung cancer, 1 case of cervical cancer, 1 case of skin cancer, and 1 ENT cancer (Fig. 1).

There were no significant sociodemographic or clinical differences at D0 between patients with and without a cancer history, notably regarding BMI (Body Mass Index, $p = 0.16$), which suggests that adiposity was unlikely to confound the observed differences in inflammatory biomarkers such as leptin, IL-6, and MCP-1.

However, significant differences were observed in the number of previous alcohol withdrawal attempts at D0 between those who had developed cancer and those who had not (5.93 ± 0.93 vs 10.86 ± 1.70, $p = 0.02$, Cohen's d = 3.03). Among inflammatory factors significantly different with the cancer parameter, a significant increase in IL-8 at D0 was observed (23.93 ± 5.35 vs 38.77 ± 10.19, $p = 0.040$, Cohen's d = 1.52) in the overall sample as well as in the unipolar depressive sample alone (24.52 ± 7.11 vs 45.23 ± 12.65, $p = 0.045$, Cohen's d = 1.71). This was confirmed in the abstinent depressive patients at M2 (22/53), where among the significantly different inflammatory factors related to the cancer parameter (5/22), a significant increase in IL-8 was observed at D0 in the depressive sample only (25.61 ± 11.00 vs 45.23 ± 12.65, $p = 0.039$, Cohen's d = 1.59). IL-8 levels remained stable compared to non-abstinent participants. IL-8 was the only inflammatory protein significantly different at D0 for the cancer parameter, and no significant differences were noted for this protein in subsequent study timepoints.

This significant difference in IL-8 at D0 was not found between abstinent and non-abstinent patients in the overall sample. However, a significant increase in TNF-alpha at D0 in favor of abstinence at M2 was noted, whether samples were studied as a whole (0.41 ± 0.09 vs 4.48 ± 1.90, $p < 0.001$, Cohen's d = 3.41), in unipolar depressive patients (0.57 ± 0.12 vs 5.66 ± 2.67, $p = 0.020$, Cohen's d = 3.35), or in bipolar patients (0.20 ± 0.07 vs 1.72 ± 0.67, $p = 0.009$, Cohen's d = 3.19). This significant increase in TNF-alpha was also present up to M6 ($p = 0.02$). TNF-alpha was the only inflammatory protein showing consistent differences associated with abstinence status at M2 over follow-up.

4. Discussion

The objective of describing our unipolar and bipolar depressive samples in the context of AUD has been achieved. The prevalence of cancer pathology was found to be over 13%, with two predominant cancers: those affecting the ENT region and breast cancer. The variety and increase in cancer types appears greater compared to our primary study, which reported a 10% cancer rate, mainly of breast cancer, among patients with psychiatric disorders. Pro-inflammatory response profiles induced by alcohol consumption in patients with psychiatric comorbidities show that IL-8 was associated with differences between patients with and without a cancer history, with higher levels in those with cancer, independent of alcohol abstinence. On the other hand, these profiles indicate that TNF-α differentiates between abstinent and non-abstinent individuals, in favor of abstinence. No statistically significant profile involving neuroplasticity, particularly BDNF, was observed, regardless of cancer or abstinence status, possibly due to the high severity of AUD and the limitations of peripheral serum measurements in capturing complex neurobiological interactions, as well as the absence of systematic control for psychotropic medications, which may have influenced inflammatory and neuroplasticity markers. Our results revealed a higher frequency of cancer compared to those in our descriptive study for patients with psychiatric disorders and AUD. This higher percentage of cancer history aligns logically with the potential impact of alcohol. Indeed, the severity of AUD in our cohort is clear, given the high number of previous withdrawal attempts (an average of over 6). The number of women is also quite significant, as in our primary cohort. The timing of the two conditions is similar, with psychiatric disorders preceding cancer onset. Cancer types are diverse in their distribution, as ENT cancers are frequent in cases of addiction, with breast cancer remaining the second most common cancer among these patients. These tumor types differ substantially in their biological characteristics, treatments, and inflammatory profiles. Cancer-related inflammatory and clinical profiles differ substantially according to age and sex, particularly in ENT and breast cancers, which were the most prevalent tumor types in this cohort [36,37]. Such tumors exhibit distinct hormonal regulation and immune microenvironments that can influence systemic cytokine expression. Consequently, age- and sex-related variability may have contributed to the heterogeneity observed in inflammatory markers in this sample. In addition, detailed information regarding disease stage or time since treatment was not systematically available. Therefore, the inflammatory differences observed should be interpreted cautiously. These findings suggest that shared inflammatory mechanisms may partly contribute to the differential IL-8 and TNF-α profiles observed in our results in relation to cancer history and alcohol abstinence. In addition, tumor-related factors such as cancer stage, disease burden, and overall severity have been shown to modulate systemic inflammatory responses, with more advanced disease associated with higher circulating pro-inflammatory cytokine levels, which may partly explain variability across clinical subgroups [38]. These elements suggest that both host-related (psychiatric and addictive disorders) and tumor-related factors jointly contribute to systemic inflammatory activation. Regarding biological results, patients with psychiatric disorders often exhibit elevated levels of pro-inflammatory cytokines, such as IL-8. A meta-analysis indicated significantly higher levels of IL-8 in depressed patients compared to healthy controls [39]. IL-8 is known for its chemotactic properties, attracting neutrophils to inflammation sites. In the context of psychiatric disorders, increased IL-8 may contribute to a chronic low-grade inflammatory state, often observed alongside other pro-inflammatory cytokines in depressive patients [40]. Additionally, elevated IL-8 plays a role in tumor progression, angiogenesis, and metastasis [41]. Accordingly, inflammatory response profiles characterized by higher IL-8 levels may be observed in patients with both cancer and psychiatric disorders compared to those with only psychiatric disorders.

In AUD, IL-8 levels have been reported to be elevated, and while these levels may decrease when patients become abstinent, they remain high compared to individuals without a history of alcohol abuse [42]. In this study, IL-8 levels did not decrease in abstinent patients, which can be partly explained by the fact that most cancer patients in the abstinent group had significantly more prior withdrawals at D0. This may reflect the greater severity of AUD in patients with cancer history, as indicated

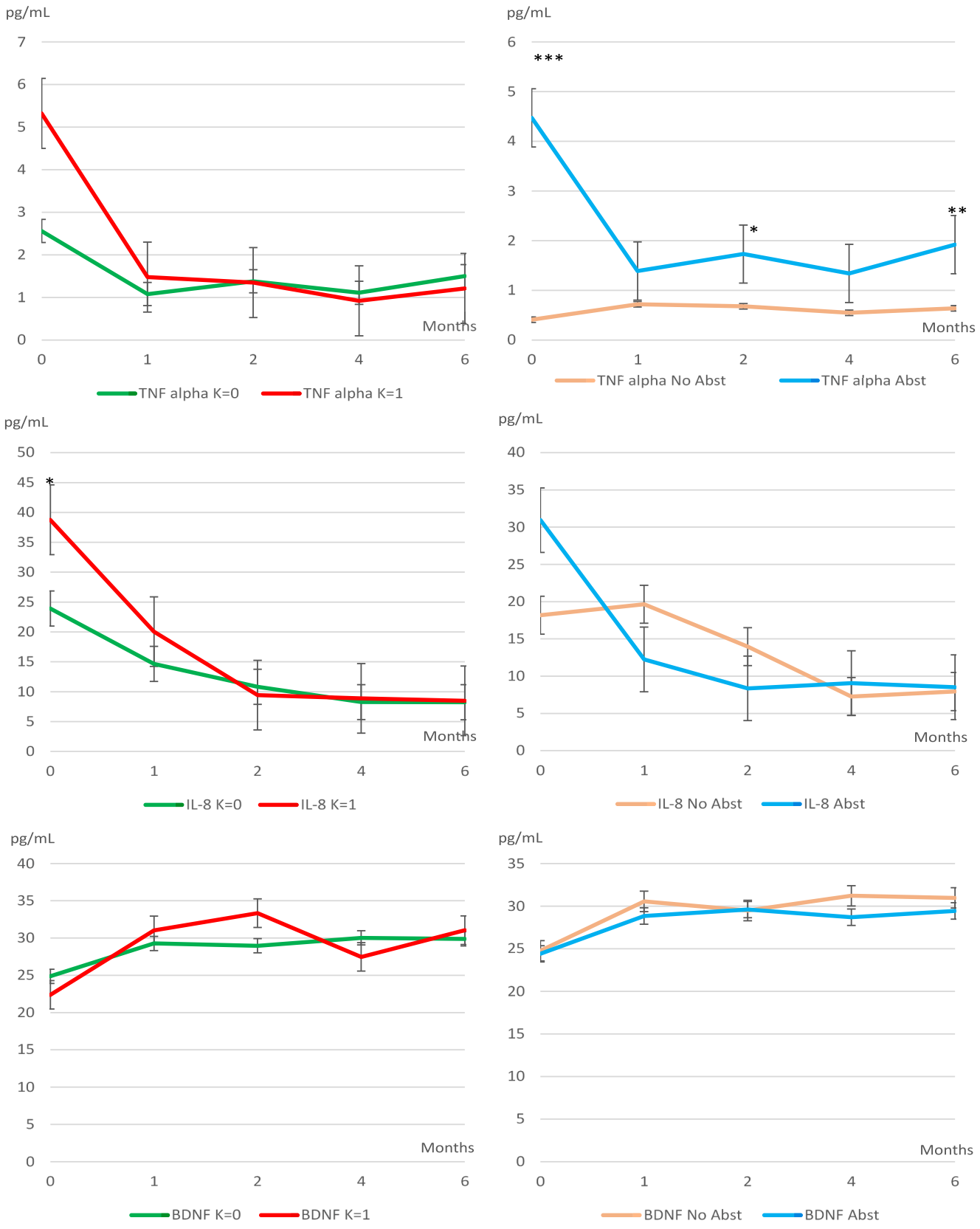

Fig. 1. Inflammatory and neuroplasticity factors under cancer and abstinence groups focus on TNF-α, IL-8 and BDNF. (Data are presented as mean ± SE (standard error); k = 0: without cancer history; k = 1: with cancer history; No Abst: non-abstinent; Abst: abstinent).

by higher prior withdrawal burden.

TNF-α is the most frequently observed marker in the literature for distinguishing between abstinence and non-abstinence, and this was confirmed in our study where it differentiated abstinent from non-abstinent individuals at M2 and remained significant until M6 [43]. Although changes in TNF-α levels have been reported with abstinence in some studies, this pattern is not consistent across populations, particularly in severe AUD cohorts. This may partly explain the observed findings.

The present study should be interpreted in light of its exploratory nature and the small size of biologically characterized subgroups, particularly participants presenting with the combination of depressive disorder, AUD, cancer history, and available biomarker data. These limited sample sizes reduce statistical power and preclude causal inference. Consequently, the findings should be viewed as hypothesis-generating rather than confirmatory.

These findings should also be interpreted within the context of European epidemiological data, particularly in French populations, where psychiatric disorders and AUD contribute substantially to cancer burden. In this framework, shared biological mechanisms, including epigenetic regulation, have been proposed to contribute to the association between psychiatric disorders, alcohol exposure, and cancer comorbidity [43]. Epigenetic modifications induced by environmental and behavioral factors such as alcohol consumption may influence both inflammatory and neuroplasticity-related processes through long-term gene regulation mechanisms. Epigenetic mechanisms may partly explain long-term modulation of inflammatory and neuroplastic pathways in the context of psychiatric disorders, AUD, and cancer.

Although most participants reported alcohol as their primary substance of use, some individuals also reported other substance use. The potential influence of these substances on inflammatory biomarkers cannot be completely excluded. CRP (C-reactive protein), a commonly used marker of systemic low-grade inflammation, was not systematically available in the present dataset. Future studies should include CRP measurements to better characterize systemic inflammatory status.

These results should be confirmed in a larger patient cohort. Additional patients meeting our eligibility criteria could be drawn from the same cohort studied here, or criteria could be applied to patients in other AUD cohorts in our biological collection, which holds blood and serum samples. Future studies should also ensure a more homogeneous characterization of withdrawal history at baseline across groups.

Another limitation is the absence of a healthy control group. The present study was conducted within a clinical cohort of patients with AUD and depressive disorders, and the primary objective was to explore biological differences within this sample rather than to compare patients with healthy individuals.

Inflammatory biomarkers such as TNF-α and IL-8 may be affected by biological, clinical and treatment-related factors including smoking status, metabolic conditions, cancer treatments, and psychotropic medications which were not systematically controlled for in the present analyses. Moreover, peripheral inflammatory and neuroplasticity-related molecules exert their effects through specific receptor-mediated pathways, meaning that circulating levels primarily reflect signaling potential rather than direct biological activity.

In addition, psychotropic medications were not systematically controlled for and may have influenced inflammatory and neuroplasticity biomarkers due to their known immunomodulatory effects. These effects are particularly relevant given the known modulation of inflammatory pathways by antidepressants and mood stabilizers. Personalized medicine should be prioritized, potentially through innovative approaches similar to molecular biology. Predictive markers to define patients' susceptibility to developing both pathologies could enable effective treatment. It would be helpful to precisely record antidepressant use, as these medications may have immunomodulatory effects that could mask certain treatment responses.

A broader sample of the target sample may help identify specific, predictive biomarkers for these chronic pathologies, individually and, more importantly, jointly. These biomarkers could be refined by incorporating epigenetic concepts, which are highly relevant for the tested markers. BDNF polymorphisms, previously examined in AUD [26,44], could be specifically targeted, as could TNF-alpha polymorphisms noted in the literature. Integrating epigenetic analyses may enhance understanding of how these biomarkers relate to both inflammation and neuroplasticity in the case of psychiatric disorders, AUD and cancer.

5. Conclusions

This study provides exploratory insights into the interplay between AUD, depressive disorders, and cancer history, suggesting potentially distinct inflammatory profiles associated with IL-8 and TNF-α. Specifically, elevated IL-8 levels were observed among patients with a cancer history, regardless of alcohol abstinence, while TNF-α was associated with abstinent status in this cohort. The findings suggest that chronic inflammation, reflected in these markers, may contribute to distinct biological profiles associated with dual diagnoses involving both AUD and depressive disorders. However, the inflammatory profile in abstinent patients did not decrease as expected, likely due to the high severity of their AUD history, as reflected by the frequent past withdrawal attempts. This underscores the need for further studies with larger, more homogeneous cohorts to validate these inflammatory markers and to explore predictive biomarkers for patients at risk of comorbid AUD, depression, and cancer. Ultimately, personalized treatment approaches integrating molecular and genetic markers may help improve understanding of inter-individual variability in inflammatory responses. Future research should also explicitly integrate epigenetic analyses and environmental factors, as these could significantly influence both inflammatory response and neuroplasticity, potentially helping to identify novel mechanistic pathways.

CRediT authorship contribution statement

Théodore Vinais: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Brigitte Plansont:** Writing – review & editing, Resources. **Alexis Parenté:** Writing – review & editing, Writing – original draft, Methodology. **Philippe Nubukpo:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Conceptualization. **Aurélie Lacroix:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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