Received: 21 December 2023 | Accepted: 2 August 2024

DOI: 10.1111/add.16658

RESEARCH REPORT

ADDICTION SSA

Predictors of substance use during treatment for addiction: A network analysis of ecological momentary assessment data

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Funding information
IReSP and Alliance Aviesan for CUSEMA study (FS), Grant/Award Number: IRESP-19-ADDICTIONS-16; IdEx "Investments for the Future" program / GPR BRAIN_2030 (MA, FS); Research Grant AAP-Recherche-CRA from the Aquitaine Regional Council (MA), Grant/Award Number: 20091301018

Abstract

Background and aims: Ecological momentary assessment (EMA) studies have previously demonstrated a prospective influence of craving on substance use in the following hours. Conceptualizing substance use as a dynamic system of causal elements could provide valuable insights into the interaction of craving with other symptoms in the process of relapse. The aim of this study was to improve the understanding of these daily life dynamic inter-relationships by applying dynamic networks analyses to EMA data sets.

Design, setting and participants: Secondary analyses were conducted on time-series data from two 2-week EMA studies. Data were collected in French outpatient addiction treatment centres. A total of 211 outpatients beginning treatment for alcohol, tobacco, cannabis, stimulants and opiate addiction took part.

Measurements: Using mobile technologies, participants were questioned four times per day relative to substance use, craving, exposure to cues, mood, self-efficacy and pharmacological addiction treatment use. Multi-level vector auto-regression models were used to explore contemporaneous, temporal and between-subjects networks.

Findings: Among the 8260 daily evaluations, the temporal network model, which depicts the lagged associations of symptoms within participants, demonstrated a unidirectional association between craving intensity at one time (T0) and primary substance use at the next assessment (T1, $r = 0.1$), after controlling for the effect of all other variables. A greater self-efficacy at T0 was associated with fewer cues ($r = -0.04$), less craving ($r = -0.1$) and less substance use at T1 ($r = -0.07$), and craving presented a negative feedback loop with self-efficacy ($r = -0.09$).

Conclusions: Dynamic network analyses showed that, among outpatients beginning treatment for addiction, high craving, together with low self-efficacy, appear to predict substance use more strongly than low mood or high exposure to cues.

KEYWORDS
Addiction, multi-level autoregression; craving; dynamic model; ecological momentary assessment; substance use disorder; symptom network

Fuschia Serre and Christophe Gauld contributed equally to this study.

INTRODUCTION

Addiction, the most prevalent psychiatric disorder in the general population, is characterized by frequent relapses. The importance of craving in relapse has been highlighted by numerous studies [1–3], and it is consequently considered as a prime target for addiction treatment. Craving appears as a central component in several addiction models [4, 5] and was introduced as a diagnostic criterion for substance use disorder (SUD) in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) [6–8]. Previous studies have explored this craving criterion among the other SUD criteria. The item response theory (IRT) method revealed that craving was the least difficult criterion and the most discriminant of all criteria when comparing across substances, suggesting its potential utility as an early indicator of SUD [9, 10]. Recent research proposes that diagnostic criteria could be dynamically and causally mutually dependent and thereby propose representation of a disorder as a network, i.e. a web of mutually influencing symptoms [11], allowing exploration of their interrelationships [12–14]. Such analysis applied to SUD criteria revealed that craving was a symptom that consistently remained in terms of centrality regardless of the substance explored, confirming its central place in the diagnosis of addiction [15].

Beyond being a diagnostic criterion (a trait), craving is primarily a dynamic state, which may vary in intensity and frequency from day to day in the same individual, under the influence of internal and environmental factors [16, 17]. One way to capture such a phenomenon is by the use of ecological momentary assessment (EMA), a method designed to collect real-time data through repeated self-reports on mobile devices, in daily life and in the natural environment [18–20]. Among participants beginning addiction treatment for different substances, previous EMA studies demonstrated that an increase of craving at one time-point was associated with a greater likelihood of substance use during the following hours [1, 21]. EMA studies have also highlighted the influence of other factors on craving and substance use/relapse (for reviews: [1, 22]). In particular, cues are stimuli previously associated with substance use and which have acquired, through learning and conditioning phenomena, the ability to induce both physiological and psychological reactivity, even in the absence of the substance [23]. A previous EMA study reported that an increased number of cues was associated with an increased craving during the following hours [21]. Interestingly, in this study, association of cues with later substance use was mediated by craving levels. Based on these results, the cues–craving–use model was proposed in substance addiction [8]. Craving and use are also influenced by other factors, including pharmacological treatment for addiction [24], self-efficacy [25, 26] and mood states [27, 28], although for this latter association different profiles emerged depending on the substance concerned [29].

Interestingly, cues, craving and their associated factors may interact and lead to relapse [30]. In this perspective, the network approach seems particularly relevant. Indeed, contrary to hierarchical linear modelling generally used to analyze EMA data [31], network models could capture, in the same model, the association between variables, considering the conditional dependence relationships of all variables. As described above, this approach allows investigating potential causal interactions between variables and, when applied to time-series data, could capture their dynamic evolution within the individual, for exploration of potential activation cascade [32]. Thus, this method offers the possibility of exploring which factors are involved, and their prospective interactions, that could lead to relapse in addiction. To date, network analysis studied the influence of pharmacological treatments on withdrawal symptoms and craving and their persistence during smoking cessation, but not controlling for the influence on subsequent substance use [33, 34].

The objective of this study was to characterize more clearly the daily life dynamic inter-relationships between substance use, intensity of craving and associated factors by way of networks analyses applied to EMA data sets. In this perspective, we hypothesized that craving would remain the main predictor of use.

METHODS

Design

The current study analyses are based on time-series data sets from two EMA studies conducted among outpatients beginning treatment: data from sample 1 (n = 163) were collected from 2009 to 2013, and from sample 2 (n = 48) from 2019 to 2022. Data from sample 1 has already been analyzed for exploring similar objectives but in a different way (see [21, 29] and Supporting information, Samples description). Study design and analysis were not pre-registered. Methodology was reported following the Checklist for Reporting EMA Studies (CREMAS) adapted for EMA protocol [35]. Both study protocols and consent forms were approved by the local ethics committee for clinical research (CPP SOOM III/DC-2009/01; CNIL/DR-2015-408; CPP IDF X: 11–2019/IR-RCB: 2018-A00952–53; CNIL MR003). Unless otherwise indicated, both studies had similar inclusion/non-inclusion criteria, procedures and assessment tools.

Participants

Individuals entering addiction treatment in the participating outpatient clinics in France were solicited for inclusion in the EMA research. To be included, participants had to be aged over 18 years, be able to read, understand and speak French fluently and to be free from any disability preventing the use of the EMA device or its understanding (e.g. severe cognitive impairment). Participants were recruited at treatment intake for a DSM-IV-TR/DSM-5 alcohol, tobacco, cannabis, opiate or cocaine use disorder of at least moderate severity (four or more criteria) for sample 1 and any severity (two or more criteria) for sample 2.

Participants received standard comprehensive care, consisting of individual behavioural treatment focused upon relapse prevention and psychosocial support combined, when available, with

pharmacotherapy [36]. After establishing a starting date, full abstinence or use reduction was encouraged as an outcome, but with no negative consequences for the individual in the case of failure to achieve this goal. Data collected for the research were not shared with medical staff.

Procedure

Inclusion

Eligible subjects who had given informed consent to participate received a 2-hour clinical interview to assess addiction severity and psychiatric comorbidity. Diagnosis of current DSM-5 psychiatric disorders were assessed using an interview adapted from the Mini International Neuropsychiatric Interview—Plus [37, 38]. Substance-related data were assessed using a validated French version of the Addiction Severity Index (ASI) [39], modified to take into account tobacco addiction [40]. The interviewer severity ratings (ISR) from the substance section, alcohol and tobacco sections of the ASI were used to assess the severity of the addiction. When multiple substance use disorders co-occurred, the substance that initiated the treatment ('primary substance') was determined according to the main problematic substance reported by the individual in the ASI.

EMA

EMA assessments started during the first month of treatment initiation. Each participant received a training session for all the EMA questionnaires delivered. At the end of the session, participants received a tablet to carry with them for 14 consecutive days (i.e. 10 weekdays and 4 weekend days). The prompting strategy used for the study was interval-based (i.e. time-based), with four random assessments per day signalled with a beep call and delivered via a time window (Supporting information, EMA procedure). The signal schedule was chosen to accommodate the participant's usual sleep schedule. Additional urine drug screen and alcohol breath tests were conducted. Financial compensation in the form of vouchers was provided depending on the number of EMA questionnaires completed (up to 100 euros for a completion rate of 75% or more).

At each EMA questionnaire, participants were evaluated with the same items:

- *Craving*. Maximum level of craving (i.e. the desire to use the primary substance) since the previous assessment was rated on a seven-point numerical rating scale: 'Since the previous assessment, have you felt the desire to use (primary substance)?' (1, 'no desire' to 7, 'extreme desire').
- *Substance use*. In this study, use referred to primary substance use (i.e. the substance at the origin of treatment request), and was collected asking: 'Since the previous assessment, have you consumed (primary substance)?' (yes/no). Additional items assessed use of any other psychoactive substances during that time-period (e.g. tobacco, alcohol, opiates, cocaine, amphetamine, cannabis or other substances).
- *Mood states*. Current mood states at each signal were rated using seven-point numerical rating scales. For the purpose of this study, only happy/sad mood states were examined, and responses were recoded into a seven-point numerical rating mood scale from 1 'very sad' to 7 'very happy' (Supporting information, EMA measures).
- *Exposure to cues*. Cues represents the total number of cues, including both substance-specific cues and person-specific cues (see [21]), encountered by the participant since the previous assessment.
- *Self-efficacy*. Self-efficacy (i.e. the degree of self-confidence in not using the primary substance) at the moment was rated on a seven-point numerical rating scale: 'To what extent do you feel able to abstain from (primary substance) use)?' (1, 'not able to abstain' to 7, 'fully capable').
- *Pharmacological treatment*. The use of pharmacological addiction treatment was collected using: 'Since the last signal, have you taken any prescribed medication for addiction? (yes/no).

Statistical analysis

Two distinct network models were conducted. A simplified network model included cues, craving and use (according to the cues–craving–use model of addiction [8, 21]). A complete network model included six variables: cues, craving, use, self-efficacy, mood and pharmacological treatments were selected according to clinical and theoretical basis, literature review of factors associated with substance use and craving in EMA studies [1] and according to a panel of research and clinical experts (M.A., F.S., L.L., E.B., J.P.D., J.A.M.F.). Models were computed pooling all substance groups, as the literature strongly suggests that craving influences substance use and relapse throughout addiction types [1, 3, 29]. However, to control for potential confounders, a sensitivity analysis testing the influence of age, sex and type of substance on the networks was implemented and is presented as Supporting information, Figure S2.

Estimation of the dynamic network models

Multi-level vector autoregression networks (mlVAR [41, 42]) were used to investigate the fluctuations of substance use and symptoms. Dynamic network models allow for investigations of within-person relationships between symptoms, while providing information regarding their temporal order and preliminary indications concerning the time windows on which they interact. Time-lagged relationships in such dynamic network models could be informative about causal relationships, denoting a variable's ability to predict another variable at

the consecutive time-point. mLVAR is a model in which all variables at a given time-point are regressed on variables of the previous assessment [42, 43]. This type of model allows estimation of three types of network, and to differentiate inter-individual effects (between-person network) and intra-individual effects (within-person contemporary and temporal networks).

First, the contemporaneous network is a Gaussian graphical model (GGM; a multi-level partial correlation network based on the residuals) that represents the within-person associations between the variables within the same window of assessment, controlled for each other and for the temporal effects. Briefly, it depicts the relationships between symptoms at the same moment, i.e. relationships between variables in the same window of measurement that cannot be explained by the temporal effects, to explore if deviations from a person's mean in two variables predict one another at the same moment [32].

Secondly, the temporal network is a directed network of regression coefficients that describes the lagged associations between symptoms from one measurement point (T0) to the next (T1, approximately 4 hours later), after controlling for all other lagged associations and autoregressive effect. It represents the average lagged within-person associations between the variables from one point in time to the next, controlled for each other. It shows whether a deviation from a person's mean predicts a deviation from the same person's mean in another variable at the next measurement occasion [44]. Feedback loops (i.e. mutually reinforcing relations) could help to reveal important patterns in how symptoms reinforce or inhibit each other over time.

Thirdly, the between-subject network is a GGM that describes the variance–covariance structure of participants' means [32, 45, 46], and represents the associations between the person-means on the variables, given the same person-means on the other variables [32]. In other words, each subject is compared to another, taking into account that their symptoms change over time.

Construction of the networks

A network contains nodes (variables) and edges (statistical relationships). The qgraph package allows the visualization of the networks [47]. The spatial configuration of the nodes in space is based on the average layout of the networks established via the Fruchterman–Reingold algorithm [48]. The networks show all the connections between nodes, while controlling for all other nodes in the network but the non-significant connections ($P < 0.001$, especially for the temporal network) are dashed. In the contemporaneous and between-subject networks, an edge is considered significant if one of the nodes significantly predicts the other and vice versa (with $\alpha = 0.05$), without correction for multiple testing [49] (Supporting information, Statistical analysis). No imputation was performed for missing data but sensitivity analyses did not show any clinically significant differences compared to networks with multiple imputations (Supporting information, Figure S3).

Inferences based on the network analysis

Network inferences were assessed with two measures of centrality outStrength and inStrength [50] used on the temporal networks. In a nutshell, centrality can be understood to reflect how connected and thus potentially clinically relevant a variable (e.g. symptoms) is in a temporal network (via paths through other variables, intervening on a highly central variable, other nodes will be both directly and indirectly affected). Strength centrality indicates the extent to which the node of a temporal network influences and is influenced by other nodes (calculated as the sum of edge weights extending out and coming into the node). A high outStrength indicates that fluctuations from one time-point to another in the central variables are the most predictive of next fluctuations in other variables. A high inStrength indicates that daily fluctuations in the central variables are the most predicted by other variables [51]. The balance of a node's out- and inStrength suggests its important role as a driving mechanistic variable of the network relative, for instance, to a passive outcome variable. According to the recommended reporting standards for network studies [52], raw centrality scores are used to avoid inflation of dissimilarity between centrality indices. We use a set of radar plots to visualize centrality metrics [53].

Softwares

Analyses were conducted with R version 4.2.2. (R Core Team, 2022) and JMP Pro (version 16.0). We used the mlVAR package (version 0.5) to estimate the three types of networks: contemporaneous, temporal and between-subject [54], and the tseries, networktools, qgraph and bootnet packages [47] to the complementary analyses and visualizations.

RESULTS

Participants

From 2009 to 2013 (sample 1) and from 2019 to 2022 (sample 2), 871 individuals who sought treatment in the participating centre met inclusion criteria for the study. Among them, 211 (24%) were included (Supporting information, Figure S1): 35% ($n = 73$) initiated a treatment for alcohol, 28% ($n = 58$) for tobacco, 18% ($n = 39$) for cannabis and 16% ($n = 34$) for opiates and 3% ($n = 7$) for cocaine. Table 1 shows a description of the clinical characteristics of each substance group.

Description of EMA reports

Among the 10 128 EMA electronic assessments delivered, 8260 (82%) were completed [39.1 prompts completed per person on average, standard deviation (SD) = 7.9] (see Supporting information, Missing data and Table S1, for missing data distribution across samples/

TABLE 1 Characteristics of the sample and description of daily life EMA variables (n = 211).

	Total sample (N = 211)			
	%	n	Mean	SD
Sample characteristics				
Sex (female)	36	78		
Employed	56	116		
Age			38.2	11.14
Education (years)			12.5	2.74
Addiction severity				
ASI ISR (0–9)*			6.6	(0.76)
MINI current diagnosis				
Mood disorder	34	72		
Anxiety disorder	45	93		
EMA variables[a]	8260 observations			
Use (of primary substance) (yes/no)	37	3087		
Craving episodes (intensity > 1)	70	5810		
Craving intensity (1–7)			3.6	2.10
Mood intensity (1–7)			4.4	1.44
Self-efficacy (1–7)			4.2	1.93
Number of cues			4.3	3.4
Pharmacological addiction treatment intake (yes/no)	34	2812		

*Interviewer severity rating (ISR) reported for primary substance in alcohol, tobacco or substance section of addiction severity index (ASI). EMA= ecological momentary assessment.
[a]Frequencies, percentages and means are based on the total number of valid electronic interviews during the assessment period.

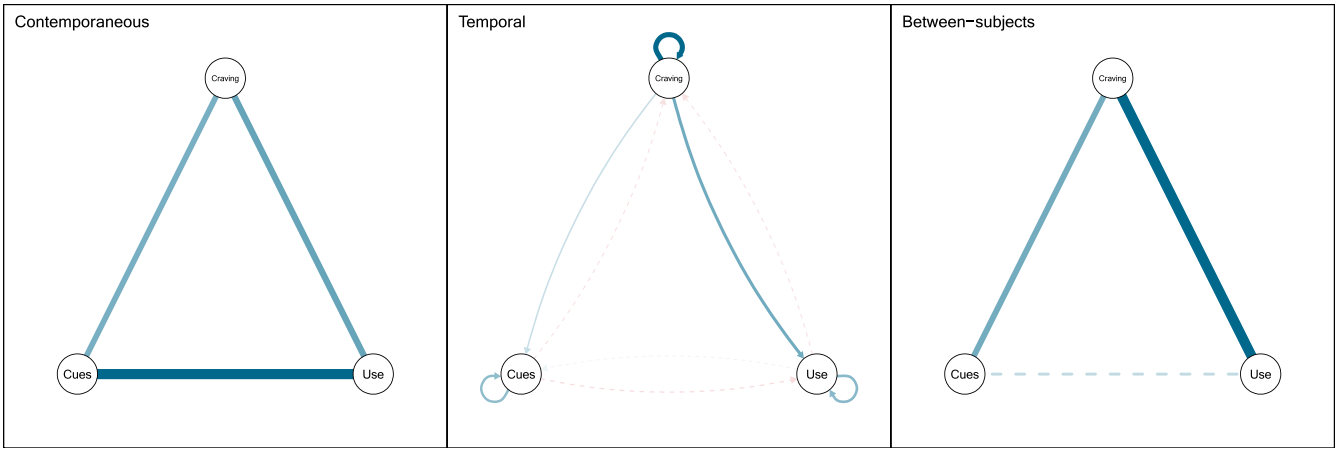


FIGURE 1 Simplified network model. Positive correlations are shown in blue, negative correlations are shown in red. Non-significant correlations are shown as dashes. The thickness of an edge represents the strength of the connection, relative to the strongest edge coefficient.

substances). Among assessments completed, use of the primary substance and episodes of craving (non-null intensity) were frequent (in 37 and 70% of assessments, respectively). The mean for craving intensity was 3.6 (2.1), 4.2 (1.9) for self-efficacy, 4.4 (1.4) for mood intensity (higher score associated with positive mood) and 4.3 (3.4) for the number of cues encountered since the last questionnaire (Table 1).

Simplified network model (Figure 1 and Supporting information, Table S2)

In the contemporaneous network, a strong cross-sectional association was observed between cues and use (r = 0.34), and a slighter but still significant association between craving and use (r = 0.20) and between cues and craving (r = 0.18).

In the temporal network, significant positive correlations were observed between craving at T0 and use at T1 (r = 0.11) and cues at T1 (r = 0.04). Positive autoregressive coefficients were identified for all three nodes (at r = 0.20 for craving, at r = 0.09 for use and at r = 0.09 for cues). The high autoregressive coefficient of craving indicates that higher craving intensity reported at T0 was associated with higher craving intensity reported at T1.

In the between-subject network, significant relationships were observed between craving and use (r = 0.57), and to a lesser extent between cues and craving (r = 0.32), indicating that participants with higher overall craving intensity are those reporting the highest number of cues, and with more frequent substance use during the study.

Complete network model (Figure 2 and Supporting information, Table S3)

In the contemporaneous network, a positive relationship was identified between cues and use (r = 0.32), and to a lesser extent between craving and use (r = 0.16) and between cues and craving (r = 0.16). Self-efficacy was negatively correlated with craving (r = −0.23) and use (r = −0.12), and higher craving was correlated with lower positive mood (or higher sadness, r = −0.09). These associations were not modified by age, sex or substance type (Supporting information, Figure S2).

In the temporal network, a positive and unidirectional prospective association was identified between craving at T0 and use at T1 (r = 0.1). Higher self-efficacy at T0 was associated with fewer cues (r = −0.04), less craving (r = −0.1) and use (r = −0.07) at T1 and to higher positive mood (r = 0.1) at T1. Interestingly, a feedback loop appears between self-efficacy and craving: an increase in craving at T0 leads to a decrease in self-efficacy at T1 that, in turn, increases craving at T2. Taking pharmacological treatment at T0 was inversely associated with craving (r = −0.04) and use (r = −0.03) at T1. Mood was not found associated with craving or use at the next assessment, but higher sadness at T0 was predictive of a higher probability of pharmacological treatment intake at T1 (r = −0.06). Surprisingly, an inverse correlation was observed between 'cues' at T0 and 'craving' and 'usage' at T1 (r = −0.04 for both). Positive autoregressive coefficients were identified for five nodes, and a negative autoregressive coefficient for the node pharmacological treatment.

In the between-subject network, the negative relationship between craving and self-efficacy was predominant (r = −0.68), indicating that people with higher self-efficacy were those with lower overall craving intensity. Self-efficacy was also negatively correlated to use (r = −0.32), but positively correlated to positive mood (r = 0.28). Participants who reported the most frequent use were also those reporting the highest number of cues (r = 0.20), more craving (r = 0.19) and more frequent intake of pharmacological treatment (r = 0.22).

Inferences based on the network analysis

Table 2 and Figure 3 describe the outStrength and inStrength centrality measures of the simplified (a, b) and complete (c, d) temporal network models. Craving and self-efficacy had a relatively high outStrength centrality, indicating that they were important variables to consider to predict other variables, and use had a relatively high inStrength centrality, which should be interpreted as the most predicted variable relative to other variables (while having a relatively large autocorrelation).

DISCUSSION

The objective of this study was to characterize more clearly the daily life dynamic inter-relationships between substance use, intensity of

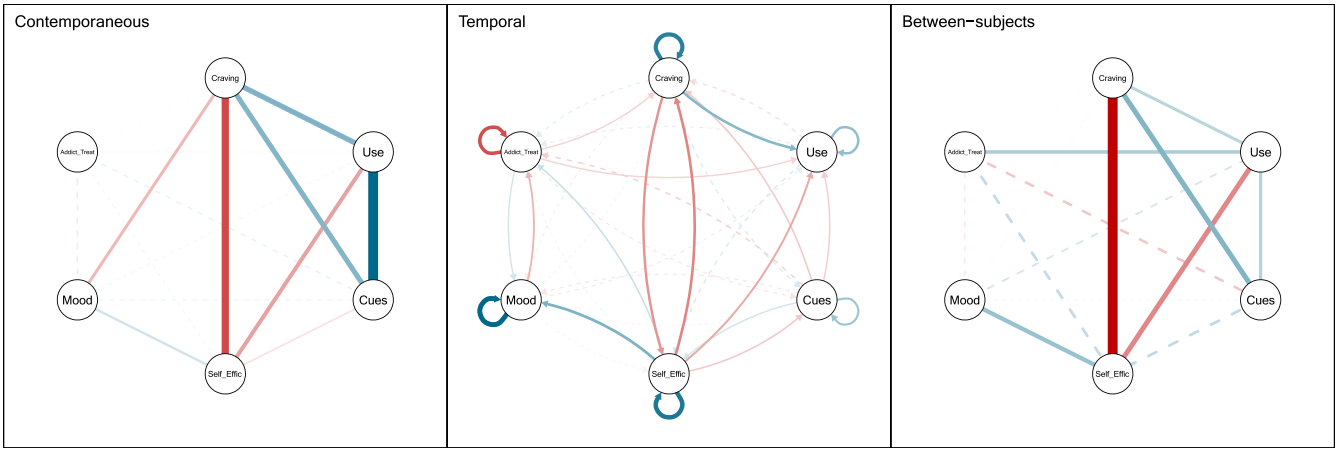
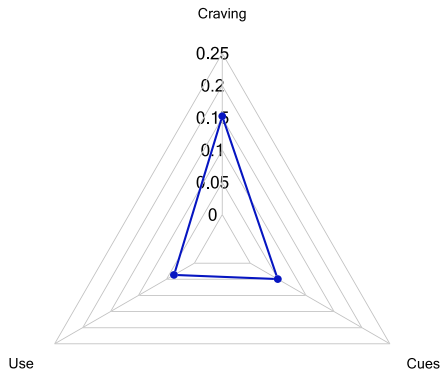


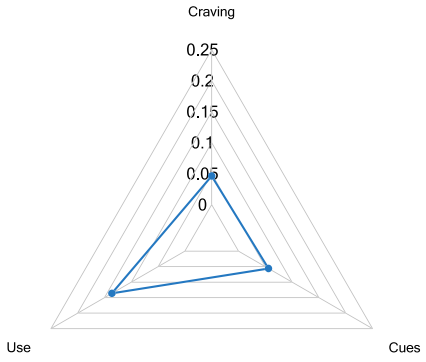
FIGURE 2 Complete network model. Positive correlations are shown in blue, negative correlations are shown in red. Non-significant correlations are shown as dashes. The thickness of an edge represents the strength of the connection, relative to the strongest edge coefficient. Self Effic: self-efficacy; Addic Treat: pharmacological treatment. Influence of age, sex and substance type was tested in sensitivity analysis and presented in Supporting information, Figure S2.

TABLE 2 Out-strength and in-strength of the complete network model. A variable with a high out-strength predicts other variables to a large extent; a variable with a high in-strength is predicted to a large extent by other variables.

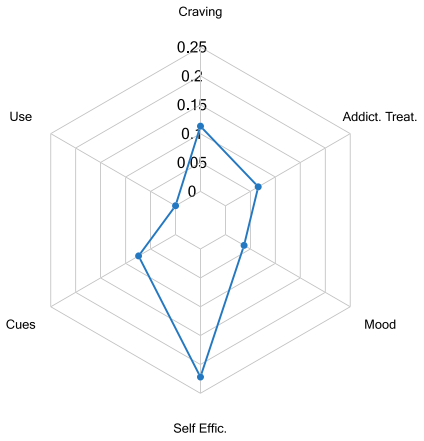
	Craving	Use	Cues	Self-efficacy	Mood	Pharmacological treatment
Out-strength	0.119	< 0.001	0.084	0.228	0.042	0.073
In-strength	0.179	0.242	0.049	0.123	0.139	0.110



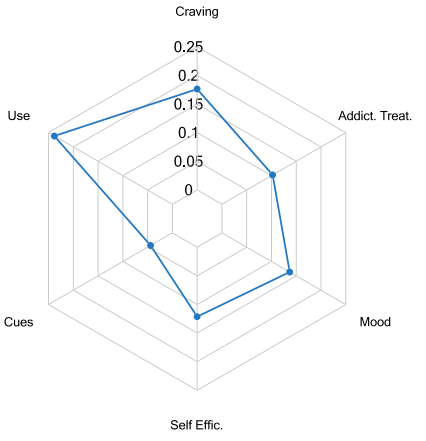
(a) OutStrength centrality for the simplified model



(b) InStrength centrality for the simplified model



(c) OutStrength centrality for the complete model



(d) InStrength centrality for the complete model

FIGURE 3 Radar plot of the centrality in the temporal simplified (a, b) and complete (c, d) network models. OutStrength centrality (represented in a, c) is the sum of all outgoing absolute edge weights from a node. InStrength centrality (represented in b, d) is the sum of all incoming absolute edge weights to a node. Self Effic: self-efficacy; Addic Treat: pharmacological treatment.

craving and associated factors by way of networks analyses applied to EMA data sets. In this perspective, we hypothesized that craving would remain the main predictor of use. The originality of this study lies in the method of analysis, which allows us to consider the joint influence of all other relationships between the network variables, and thus to explore in more depth the mediating role of some of them, and to examine the possible cascades of activation that could lead an individual to relapse.

In the simplified model (based on the cues–craving–use model of addiction [8]), cues, craving and primary substance use were highly inter-related when reported at the same assessment. The strong association between cues and substance use seems relatively predictable, as cues were derived from an individual's specific objects, circumstances or environmental contexts that were commonly paired with its own substance use [21]. As a second step, the temporal network explored prospective associations to approach possible causal relationships between the variables. Results confirmed the unidirectional association between increased craving at one time and higher probability of substance use at the next assessment. Similar results were previously observed in the same data set when analyzed with hierarchical linear modelling [21] and among other EMA data sets using multi-level modelling [1]. Compared to other methods, dynamic

network analyses explore these associations by simultaneously considering all the influences of the other variables integrated into the network, as well as the auto-influence of a variable (autoregression). In this temporal model, the absence of links between cues and substance use confirms the mediating role of craving, as previously highlighted [21]. This result confirms the major prospective role of craving in substance use [3], and therefore the importance to target craving for relapse prevention in addiction treatment.

In the complete model, variables known to potentially impact craving and/or substance use were added to explore their relative implication in use that could represent potential levers of action for addiction treatment. The temporal network highlighted (1) that substance use was mainly predicted by higher craving at the previous assessment and (2) the unidirectionality of this association, as substance use was not significantly predictive of later craving in this model. This observation was also supported by centrality measures, with a high outStrength centrality for craving, indicating that it predicted other variables to a large extent and, conversely, high inStrength centrality for substance use, indicating that it was the most predicted by other variables.

The complete temporal network also highlighted influence of self-efficacy. Previous studies have reported an inverse correlation with substance use, and hypothesized that self-efficacy could moderate the link between high-risk situations for substance use and relapse [55]. In our study, higher self-efficacy predicted less substance use at the next assessment, after controlling for the influence of other variables in the network (including craving), suggesting that this effect was partly independent of the way the individual manages exposure to cues or craving. Higher self-efficacy also predicted, at the next assessment, less craving (with a negative feedback loop), fewer cues, less negative mood and more frequent intake of pharmacological treatment. From a clinical viewpoint this is a major finding, highlighting the fact that craving and self-efficacy are two key and independent factors contributing to substance use, and must therefore be targeted and treated together to effectively prevent relapse.

Another important result is that the use of a pharmacological treatment at T0 was associated with less craving and less substance use at T + 1, but also with a higher positive mood. This result confirms their effectiveness for treatment of addiction, and is consistent with previous results [33].

Conversely, some links presented surprising associations. This is particularly the case for the negative association between cues at T0 and craving at T1 in the complete network model. This result may be explained by the fact that the temporal sequence between exposure to cues and craving is almost instantaneous, and therefore is captured more effectively by the contemporaneous network. The absence of this association in the simplified model, in contradiction with previous findings [21], may be explained by the adjustment on influence of substance use, which could be a potential confounder. Another finding concerned the absence of a prospective association between mood and craving or use. Affect and emotion regulation have frequently been proposed as an important motivation for alcohol/substance use (i.e. to cope with negative affect or to enhance positive affect [56–58]), and is associated with craving [59]. However, time-series data have made it possible to explore more precisely, and to nuance, the relationships at the within-person level [27, 60]. A previous dynamic network study showed a unidirectional prospective association between craving and sadness during smoking cessation [34]. This suggests that negative affect could be explained by craving itself, which represents a state of high stress marked by emotional distress [61]. This would be in line with the cross-sectional correlation observed in the contemporary model between craving and negative mood.

Some limitations must be acknowledged. The first concerns the way the variables were measured. Single-item measures are particularly effective in EMA [62], but we cannot rule out that multi-item measures could have provided different results. EMA assessments were spaced at an average of 4 hours apart, which limited interpretation for more rapid sequences of events. Secondly, we cannot exclude that the addition of other variables could have modified the observed relationships. However, variables were selected based on clinical expert opinion and literature reviews on factors associated with substance use and craving [1]. Thirdly, the database analyzed was built on two distinct samples, collected during two different time-periods (2009–13 and 2019–22). Although the places of recruitment were similar between the two samples, we cannot exclude the possibility that there may have been changes in inclusion and/or addiction management procedure between these two periods, as suggested by the difference in self-efficacy and mood EMA reports observed (Supporting information, Samples differences in EMA scores). Fourthly, only a minority (24%) of patients eligible for the study was included (see Supporting information, Figure S1, Supporting information, Samples description), due primarily to not attending inclusion visits. It is important to note that the present observations can be generalized only to individuals who seek treatment for an addiction. Fifthly, participants' reactivity to EMA methodology was not explored in this study. However, previous studies did not reveal any influence on relapse rates [63], even if more frequent assessments have been associated with less craving [64], in line with the potential therapeutic effect of self-assessment [65]. Lastly, in this study we were particularly interested in associations derived from the temporal networks, as edges could be informative about which variable temporally precedes another in a system. However, it is important to note that prospective relationships are not sufficient for a full demonstration of causal processes as it only satisfies a temporal criterion, and are best interpreted in terms of predictive capacity [44].

In perspective, the widespread use of smartphone applications should make it easier to collect such longitudinal data and provide a unique opportunity to understand more clearly how these interrelationships evolve over time [66], as well as the condition under which treatments are effective, by highlighting the variables that act as levers, as well as any potential obstacles [34, 67]. For example, when repeated at several points during the course of a treatment, such analyses could inform regarding the variables improved by treatment and those that still need to be treated. Interestingly, such dynamic symptom network analysis can also be applied at the level of

the individual [54, 68], and contribute to the development of precision and personalized medicine.

Taken together, these results illustrate how dynamic network analysis can be applied to time-series data to explore the cascade of activation of different symptoms/events leading to substance use and relapse in addiction. The current study showed that high craving, together with low self-efficacy, were the most predictive factors of substance use in outpatients beginning treatment for addiction, and that these effects were more important than the influence of cues, mood or pharmacological treatment. These findings have important implications for addiction treatment, as they highlight that craving and self-efficacy are two key and independent factors contributing to substance use, suggesting that they need to be targeted together to effectively prevent relapse.

AUTHOR CONTRIBUTIONS

Fuschia Serre: Conceptualization (lead); data curation (equal); formal analysis (equal); funding acquisition (lead); investigation (equal); methodology (lead); project administration (lead); software (supporting); supervision (lead); validation (equal); visualization (supporting); writing—original draft (lead); writing—review and editing (lead). **Christophe Gauld:** Conceptualization (lead); data curation (equal); formal analysis (lead); methodology (lead); software (lead); validation (equal); visualization (lead); writing—original draft (lead); writing—review and editing (lead). **Laura Lambert:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); software (supporting); validation (equal); visualization (supporting); writing—original draft (supporting); writing—review and editing (equal). **Emmanuelle Baillet:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); software (supporting); validation (equal); visualization (supporting); writing—original draft (supporting); writing—review and editing (equal). **Virginie Beltran:** Investigation (equal); writing—review and editing (supporting). **Jean-Pierre Daulouede:** Resources (supporting); writing—review and editing (supporting). **Jean-Arthur Micoulaud-Franchi:** Conceptualization (supporting); writing—review and editing (supporting). **Marc Auriacombe:** Conceptualization (equal); funding acquisition (lead); methodology (equal); project administration (lead); supervision (lead); writing—review and editing (lead).

ACKNOWLEDGEMENTS

This study received financial support from: Research Grant AAP-Recherche-CRA (20091301018) from the Aquitaine Regional Council (M.A.) for Sample 1, IRESP-19-ADDICTIONS-16 from IReSP and Alliance Aviesan for CUSEMA study (F.S.) for Sample 2, French government in the framework of the University of Bordeaux's IdEx 'Investments for the Future' program/GPR BRAIN_2030 (M.A., F.S.) for the current analysis. Office and staff support was provided by CH Charles Perrens and University of Bordeaux. Melina Fatseas and Joel Swendsen are acknowledged for their contribution to the Sample 1 EMA study. The authors express theirs thanks to all participants for their contribution, and are grateful to all the interviewers of the Addiction Team of SANPSY lab 2009-2022.

DECLARATIONS OF INTEREST

None to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Serre F, Gauld C, Lambert L, Baillet E, Beltran V, Daulouede J-P, et al. Predictors of substance use during treatment for addiction: A network analysis of ecological momentary assessment data. Addiction. 2024. https://doi.org/10.1111/add.16658