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Network analysis of substance abuse and dependence symptoms

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ABSTRACT

Background: The DSM uses one set of abuse and dependence criteria to assess multiple substance use disorders (SUDs). Most SUD research aggregates across these symptoms to study the behavior of SUD as a static construct. We use an alternative approach that conceptualizes symptoms as directly interacting variables in psychopathological networks. We apply network models to symptom-level data to investigate the unique roles of individual symptoms and their interactions in SUD.
Methods: We analyzed 11 DSM III-R/IV abuse and dependence criteria in a sample of 2405 adult twins who reported use of at least one illicit substance six or more times from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD). We estimated a symptom network for each substance class as well as a global network collapsed across all substance classes. We examined similarities and differences across the 6 networks in terms of symptom-to-symptom connections and symptom centrality.
Results: The global network model revealed several interesting symptom connections, such as a strong predictive relation between tolerance and more-than-planned substance use. The most central symptom was using a drug more than planned. In addition, several interesting differences across substances emerged, both in the strength of symptom connections as well as the centrality of symptoms to each network.
Conclusions: When analyzed as networks, abuse and dependence symptoms do not function equivalently across illicit substance classes. These findings suggest the value of analyzing individual symptoms and their associations to gain new insight into the mechanisms of SUD.
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1. Introduction

Drug abuse and dependence is a common and increasing worldwide public health concern (World Health Organization, 2010). In the US, life-time prevalence estimates of substance use disorders (SUD) range from 2–3% for illicit substances to 8% for alcohol use, and 12-month rates of substance abuse or dependence increase from 7% to 20% during adolescence (Merikangas and McClair, 2012).

Recent research in psychopathology indicates that the analysis of individual symptoms can reveal crucial insights obfuscated by other analytic strategies (Fried and Nesse, 2015; Smeets et al., 2014). A central tenet of symptom-based approaches is that interactions among symptoms may be central to understanding how disorders arise, sustain themselves, and are cured (Borsboom and Cramer, 2013; Buu et al., 2012; Cullen et al., 2013; Fergus et al., 2015; Fried, 2015; Jacobsen et al., 2001). A useful way to examine such symptom-level effects is to apply a *network model*, which uses pairwise interactions among symptoms to represent a disorder as a web of mutually influencing symptoms (Borsboom and Cramer, 2013). These models have been successfully applied to a number of disorders such as posttraumatic stress disorder (McNally et al., 2015) and major depression (Fried et al., 2015).

The network framework is an appropriate and useful conceptual approach to analyzing data whenever relations among symptoms can be plausibly interpreted as interacting directly with each other. Similar to other disorders, there is evidence that SUD symptoms may arise in a causal sequence; for example, drinking more alcohol than planned is frequently the first symptom of alcohol use

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disorder to arise (Buu et al., 2012), which aligns with the finding that impaired control over alcohol use is an important predictor of problem drinking in adolescents (Leeman et al., 2012). To date, no research has investigated such symptom interactions. A network model of SUD can give an overview of the connection patterns among symptoms, revealing which symptoms are most closely related to each other, and which symptoms are most central to the disorder. In addition, network analyses allow us to compare networks across several substance classes, and to locate important differences in the symptom-to-symptom pathways that may exist due to distinct pharmacologic and psychological properties of the substance and/or different patterns of use (Degenhardt et al., 2001; Koob and Le Moal, 2006).

In the remainder of the paper, we present and interpret three cross-sectional network analyses of substance abuse and dependence symptoms. First, we examine a psychopathological network of symptom data averaged over 6 illicit substance classes (cannabis, sedatives, stimulants, cocaine, opioids, and hallucinogens) in 2,405 individuals. We investigate the pairwise connections among 11 symptoms, and estimate measures of symptom centrality to identify which symptoms may be most important in the maladaptive behavior patterns of SUD. Second, we compute symptom networks for each of the substance classes separately. Our aim here is to explore the important differences and similarities of substance classes based on a network representation, and what these differences can tell us about the interconnectivity patterns of SUD symptoms. Finally, we estimate the variance of symptom-to-symptom connections across substance classes (i.e., how much does the strength of the association between symptom pairs vary across the six classes) to identify which of these connections vary most widely across substances.

Table 1
Substance abuse and dependence criteria used to determine diagnostic status for each substance use disorder.

Variable	Criterion
A1	. . . did you often use it when you were doing something important like being at school or work or taking care of children? . . . did you stay away from work or school or miss appointments because you were using it?
A2	. . . did you ever use it in a situation in which it might have been dangerous?
A3	. . . did you have legal problems or traffic accidents because you were using it?
A4	. . . did your use of it cause problems with other people such as family members, friends, or people at work?
D1	. . . did you find that you needed to use a lot more in order to (get high/feel its effects) than you did when you first started using it?
D2	. . . did you ever have withdrawal symptoms—that is feeling sick when you cut down or stopped using it? . . . did you often use it to keep from getting sick (with withdrawal symptoms)?
D3	. . . did you often find that when you started using it, you ended up taking much more than you had planned?
D4	. . . did you try to cut down or stop using it?
D5	. . . did you spend a lot of time taking it or recovering from using it, or doing whatever you had to do to get it?
D6	. . . did you use it so often that you would use it instead of working or spending time on hobbies or with your family or friends?
D7	. . . did your use of it cause physical problems or make you depressed or very nervous?

Note: the question stem for all items was, "During that time when you were using [drug] the most, . . . ". Variables A1 and D2 were formed by collapsing two highly similar items; if either item was positively endorsed, the collapsed item was scored as endorsed.

2. Method

2.1. Sample

Data for the analyses carried out in this study come from twins who participated in the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD). Initial eligibility was determined through successful matching of birth records, if twin members were Caucasian and born between 1940 and 1974 in Virginia, USA. Detailed information about substance use and related behaviors were obtained for 2 data collection samples. Female–female twins participating in the third follow-up (Wave 4, $N = 1928$ individuals interviewed by phone in 1995–1997) and male–male and male–female twins from the first follow-up (Wave 2, $N = 5{,}602$ individuals personally interviewed in 1994–1998) served as the sample pool of twins with valid substance use data. These interviews included assessments of lifetime drug use and items worded according to the DSM abuse and dependence criteria for six categories of substances that were administered using an adaptation of the Structured Clinical Interview (SCID; Spitzer et al., 1987). Drug classes were defined as follows: cannabis (e.g., marijuana and hashish); sedatives (e.g., quaalude, Seconal and Valium); stimulants (e.g., speed, ecstasy and Ritalin); cocaine (intranasal and crack); opioids (e.g., heroin and morphine); and hallucinogens (e.g., LSD and PCP). Of the sample pool of 7530 twins (44% female, age range 20–63, mean age = 36.8, SD = 8.9), 2405 reported having used at least one of the six substances more than 6 times during his or her life and were therefore retained for analysis.

The eleven SUD criteria are presented in Table 1. Each participant, based on his responses to the usage items, was asked to respond to some or all of the 4 abuse and 7 dependence criteria for each substance class using a 3 point response scale. The response options included two positive choices (e.g., "definitely" and "probably") and one negative response ("no"). The individual symptoms were always asked for the time period in the respondent's life when they were using that drug class the most. For the analyses reported here, responses were re-coded into binary variables[1] by collapsing over the two positive response options.

2.1.1. Missing data. The analysis sample for each substance class included only those participants who reported having used the substance 6 or more times. These participants were asked to indicate whether they had ever used the substance at least 11 times during a single month. Participants who reported not having used a particular substance 11 times in a month were administered the set of abuse items (i.e., A1–A4), and were then administered the set of dependence items (i.e., D1–D7) only if they positively endorsed at least one of the abuse symptoms. For all analyses reported here, missing values generated by this imposed structured skip out were set to zero, indicating an implied negative response for each skipped item. Participants who reported having used a substance 11 times in a month were administered all abuse and dependence items. Table 2 displays the number of participants falling into each of these categories (i.e., 6 or more lifetime uses, endorsement of at least one abuse criterion, and 11 or more uses in a month) for each substance class. In addition to the structured skip-related missingness, 41 individuals had additional item-level missing data; these cases were deleted.

[1] There are two reasons for dichotomizing the responses. First, the category 'probably' was, on average, much less endorsed than the other two, leading to small cell optimization problems. Second, the behavior of potentially skewed polytomous variables in network models is not well understood at present.

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