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## Identifying viable theoretical frameworks with essential parameters for real-time and real world alcohol craving research: a systematic review of craving models

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### ABSTRACT

**Background:** Substance use is known to be episodic, dynamic, complex, and highly influenced by the environment, therefore a situational and momentary focus to alcohol craving research is appropriate. Current advances in mobile and wearable technology provide novel opportunities for craving research. However, the lack of consensus within craving theory impedes the identification and prioritization of parameters to be monitored. The aim of this study is to critically review current craving models in order to determine viable theoretical frameworks of alcohol craving and its essential parameters.

**Methods:** Eighteen models of craving were reviewed by applying a literature search with a five-step strategy that accounted for the momentary nature of craving and included a snowballing search and a key term extraction algorithm. Based on this review, multiple decision criteria were defined upon which to evaluate the models.

**Results:** Six models for alcohol craving were supported by sufficient empirical research to be eligible. The inferences drawn on these six models resulted in three decision criteria: the model should (1) incorporate negative affect as a predictor of relapse; (2) explain that dependent drinkers have a higher attentional bias towards alcohol cues than nondependent drinkers; (3) incorporate increased risk of relapse with heightened stress levels.

**Conclusions:** The affective processing model of negative reinforcement, the cognitive processing model, the incentive sensitization theory of addiction and the theory of neural opponent motivation are classified as viable theoretical frameworks, resulting in negative affect and stress as relevant parameters to include in real-time craving monitoring research.

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Alcohol craving; relapse; negative affect; stress; attentional bias; alcohol cues

## Introduction


Craving, defined as the subjective, unwanted desire or urge to use a substance while attempting to abstain (Serre et al. 2015), is generally considered a fundamental precursor to relapse in alcohol addiction (Rohsenow & Monti 1999). Many patients and clinicians in addiction care regard craving as a highly challenging obstacle for achieving recovery (Lowman et al. 2000). Although cognitive-behavioral treatment offers patients useful relapse prevention techniques, patients frequently fail to apply these consistently or timely since they often simply do not recognize their high-risk (re)lapse situation (Larimer et al. 1999). Rohsenow and Monti (1999) state that making patients aware of their craving in high-risk situations may protect them from relapse by prompting them to mobilize their coping resources. Current advances in mobile (Serre et al. 2015) and wearable

technology (Shiffman 2009) provide novel opportunities for craving research to detect such high-risk situations, by enabling continuous real-time monitoring in natural environments (Intille 2012).

Shiffman (2009) argues that since substance use is known to be episodic, dynamic, complex, and highly influenced by the environment, a situational and momentary focus to evaluate theory would be natural. However, this situational (or ecological) and momentary approach in research is novel and the number of studies in craving research is still limited (Serre et al. 2015). As a result, not much is known yet about how craving relates to substance use in real-time in the real world (Wray et al. 2014). In fact, most craving research so far has been carried out in a laboratory setting (Drummond 2001). Drummond (2001) argues that short-term, cue-elicited responses may be more relevant to predict relapse than withdrawal or background variables related to craving. He states

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that little attention has been paid to this dynamic character in existing craving measures, with only a few examples of studies using ecological momentary assessment. Concluding, real-time monitoring in a person's natural environment has great potential for both craving research and addiction treatment.

Before being able to apply real-time ecological monitoring in craving research, the essential parameters in this real-time process of craving need to be identified. However, a lack of consensus on a definition for the concept of craving, and the multitude of available theoretical models with numerous variables (Skinner & Aubin 2010) impedes the identification and prioritization of relevant parameters. Therefore, the present study aims to critically review the current alcohol craving literature in order to select the essential parameters to include in real-time ecological alcohol craving research. With a focus on the process of craving and relapse in persons with alcohol addiction, in contrast to the process of developing an addiction. To achieve this objective, a theory-centered approach was adopted in which craving models are reviewed.

For this concise, yet comprehensive review, we employed a heuristic review methodology to disclose the most relevant evidence efficiently. Applying a more common, exhaustive review methodology (e.g. Higgins and Green (2011)) would be practically infeasible for the purpose of our review, due to both the sheer quantity and the heterogeneity of evidence to be considered. As a first step, we reduced the number of models to be included by starting with Skinner and Aubin's review (Skinner and Aubin 2010), which was built on earlier reviews by Tiffany (1999) and Drummond (2001).

### Models of alcohol craving

Skinner and Aubin (2010) classified 18 craving models into four categories: conditioning, cognitive, psychobiological and motivational. These models reflect that craving is: (1) a multidimensional construct, (2) examined by a variety of scientific disciplines, yet (3) no model appears to be clearly better than all the others (Drummond 2001). These 18 models are listed in Table 1.

The review of Skinner and Aubin is primarily a descriptive taxonomy of craving models without the aim of providing a ranking among them, leading to difficulty in choosing a viable theoretical framework. As can be seen in Table 1, for several models the authors provided no criticisms. Either this implies a lack of available evidence for a critical appraisal of these models, or Skinner and Aubin's (2010) review may have lacked sufficient rigor in retrieving relevant evidence in support of these models. Here, we build on their work by systematically disclosing the empirical evidence for all these models in an attempt to identify viable theoretical frameworks. Of the 18 models, the four conditional models were excluded a priori since Skinner and Aubin (2010) convincingly argued that the assumption that craving is merely a conditioning concept has been disproven.

### Material and methods

To test the validity of the fourteen remaining models, decision criteria were determined. These decision criteria served

as assessment rules to critically evaluate model assumptions against the empirical evidence. These decision criteria were derived from two sources.

First, the existing criticisms by Skinner and Aubin (2010) presented in Table 1 were reformulated into decision criteria. Second, decision criteria were derived from empirical evidence, as outlined in the *Literature Search Strategy* section. After defining these decision criteria, an empirically based evaluation of the models can be made and viable theoretical frameworks of craving are determined. The procedure to arrive upon this framework based on the decision criteria is described in the '*Determining Viable Theoretical frameworks*' section, and graphically depicted in Figure 1. After determining viable theoretical frameworks of craving, parameters are retrieved from the models. These parameters are assessed on relevance for the dynamic and fluctuating character of craving, which is further explained in the '*Selecting Parameters for Real-time Ecological Craving Monitoring*' section.

### Literature search strategy

Due to the wide scope of this review, a more selective rather than exhaustive search strategy was employed. The aim of this strategy was to find relevant empirical studies for each model, which assessed the validity of the corresponding model assumptions. We assumed that researchers who are investigating model assumptions referenced its original founding publication. The article search could consequently be restricted to snowballing through the citations of these founding publications, instead of having to search through all articles available. However, due to the high number and heterogeneity of articles retrieved, simply including all articles found through snowballing was still infeasible. To further restrict the number of relevant articles, the articles were classified into homogeneous groups of content through key term classification (Siddiqi & Sharan 2015). A key term classification algorithm generated a frequency table of key terms per model found in the retrieved articles. Articles containing a high frequency key term (found in more than four articles) were then included for reviewing. This threshold increased the likelihood of making relevant inferences based on multiple empirical studies instead of a single one. This threshold of four articles seemed to be a relevant cutoff, considering that nine was the next number of articles found for a keyterm. We used the collective results of the empirical studies within a homogeneous group of content, to draw inferences on the validity of the model assumption related to that content.

Summarizing, a 5-step search strategy was used, consisting of a combination of snowballing and a subsequent key term extraction algorithm, as follows:

1. *Searching articles citing the founding publication.* According to Greenhalgh and Peacock (2005), a snowballing approach is the most efficient way of collecting articles in a literature review. The snowballing method was applied by searching Scopus for all articles citing the founding publication of each model up to 26 April 2016.
2. *Applying exclusion criteria.* Articles found in the preceding step, were excluded if they met one of the following

**Table 1.** Descriptions of craving models, as reviewed by Skinner and Aubin (2010). The left column presents the model name and its founding publication as identified by Skinner and Aubin (2010). The central column briefly describes the model, and the right column shows Skinner and Aubin's (2010) critical appraisal of the various models.

Model	Description	Criticisms of Model according to Skinner and Aubin (2010)
<b>Conditioning-based Models</b>		
1. Withdrawal model Wikler (1948)	Symptoms of withdrawal become associated with a stimulus. As a result, this stimulus will result in an urge to drink to relieve these withdrawal symptoms.	'These [conditional] models were discredited, (...) by numerous studies that found fault with some of their basic assumptions' (p. 609).
2. Compensatory model Siegel (1983)	Over time an addict develops tolerance, this leads to a contrary reaction rather than the pleasure of the substance. Craving occurs to escape this process of discomfort.	"
3. Opponent-process model Solomon and Corbit (1974)	Craving is a stimulation to use the substance and to give relief from withdrawal symptoms.	"
4. Incentive model Stewart et al. (1984)	Craving promotes individuals to seek the substance as a reward. An addict experiences pleasure just by thinking of the expected reward.	"
<b>Cognitive models</b>		
5. Outcome expectancy model Marlatt (1985)	Environmental cues can trigger powerful expectations about the effects of alcohol. These expectations can be a craving for reward or relief. This craving can be followed by urge, which is the actual intention to drink.	'Little research exists to validate the outcome expectancy model and the attempts to confirm the theory have not been conclusive perhaps because more specifications of the features of the model are needed' (p. 610). 'The relationship between outcome expectancies and urges, however, is still unknown' (p. 610).
6. Dual-affect model Baker et al. (1986)	This model assumes that craving can be induced by a positive or negative affect, but not together. Negative affect craving can be triggered by: (1) negative emotions, (2) aversive events, (3) withdrawal or cues associated with withdrawal, and (4) no availability of an alcohol cue. Positive affect craving can be triggered by: (1) positive emotions, (2) small alcohol dosage, (3) cues paired with alcohol use, or (4) availability of an alcohol cue.	'Baker et al. (1986) admitted that it did not explain why some drug users do not become addicted' (p. 611). '(...) they had primarily considered data from smoking studies, reducing the theory's external validity' (p. 611). 'One challenge to the model is that the induction of positive mood states generally did not affect urge when cues were not presented' (p. 611).
7. Affective processing model of negative reinforcement Baker et al. (2004)	Craving occurs to escape from the negative effect of withdrawal symptoms. This effect is increased by additional stressors.	'Some addicts relapse long after withdrawal symptoms should have ceased' (p. 611). 'The relief of aversive withdrawal symptoms cannot be an important determinant of addiction because some drugs (e.g., tobacco, cocaine, and buprenorphine) are highly addictive without producing highly unpleasant syndromes' (p. 611).
8. Cognitive processing model Tiffany (1999)	Alcohol use is an automated conditioned process for an alcoholic who is not trying to quit. Only when the process is blocked by a situation (for example, when a bar is closed) is a non-automatic process activated which then causes craving. The process can also be blocked by a person's attempt to abstain from alcohol.	No criticisms reported.
<b>Psychobiological models</b>		
9. Three-pathway psychobiological model Verheul et al. (1999)	Three types of craving come from three causes, which all have their individual neurobiological process: need for reward (dopamine/opioidergic dysregulation), need for relief (GABAergic/glutamatergic dysregulation), and lack of control (serotonergic dysregulation).	'Verheul et al. equate craving with the intention to consume, they do not attempt to explain how craving occurs without consumption (a frequent occurrence in treatment units) or, for that matter, how consumption occurs without craving' (p. 614).
10. Incentive sensitization Robinson and Berridge (1993)	A psychological process termed 'incentive salience' occurs, which is the increase in the perceived value of the substance, making the substance more attractive and the craving stronger.	No criticisms reported.
11. Theory of neural opponent motivation Koob and Le Moal (1997)	A combination of the (1) Incentive sensitization model, (2) Opponent-process model and (3) Affective processing model of negative reinforcement, this theory integrates the processes of sensitization, counter adaptation and the predominance of the influence of negative affect.	No criticisms reported.
12. Temporal-difference reinforcement learning model Redish (2004)	Actions are selected that maximize future reward and a person learns the reward value of each action. Drugs influence this learning process causing a person to choose actions leading to rewards of drug-use over non-drug-use.	'The model explains how an addict over-selects actions that lead to probable use, but it is yet to be empirically proven' (p. 613).

(continued)

Table 1. Continued

Model	Description	Criticisms of Model according to Skinner and Aubin (2010)
13. Unified framework for addiction Redish et al. (2008)	Craving is caused by a change in the allostasis and an overvaluation of the outcome and the reward of drug use.	'Several peer commentators have pointed out a major omission which is the absence of affective processes as a vulnerability' (p. 614). 'The overvaluation of the habit system (vulnerability 7), (...) which has not been empirically proven' (p. 614).
14. Neuroanatomical model Anton and Carolina (1999)	Chronic alcohol exposure leads to sensitization, which can contribute to a subjective feeling of discomfort and craving during abstinence. Stress can enhance this process and trigger reward memory.	No criticisms reported.
15. Model of interoceptive dysregulation Paulus et al. (2009)	Drug-use itself is a repeated perturbation of the current body state, which becomes associated with conditioned stimuli that contribute to the sensitization of the body prediction error. Craving comes from the motivation to use drugs and interoceptive body sensations.	No criticisms reported.
<b>Motivational models</b>		
16. Motivational model of alcohol use Cox and Klinger (1988)	Drinking is fundamentally a choice. Persons choosing to drink are motivated by their expectations that their current affect state will improve.	'The model accounts less well for the irrational aspects of craving in the alcohol dependent' (p. 618).
17. Multidimensional ambivalence model Breiner et al. (1999)	Approach (craving) and avoidance are two pathways in the brain that respond independently to various moderators.	No criticisms reported.
18. Prime theory West and Hardy (2006)	There are two moderators of craving, namely impulses and motives.	'What remains to be accomplished is the validation of hypotheses generated by this model' (p. 620).

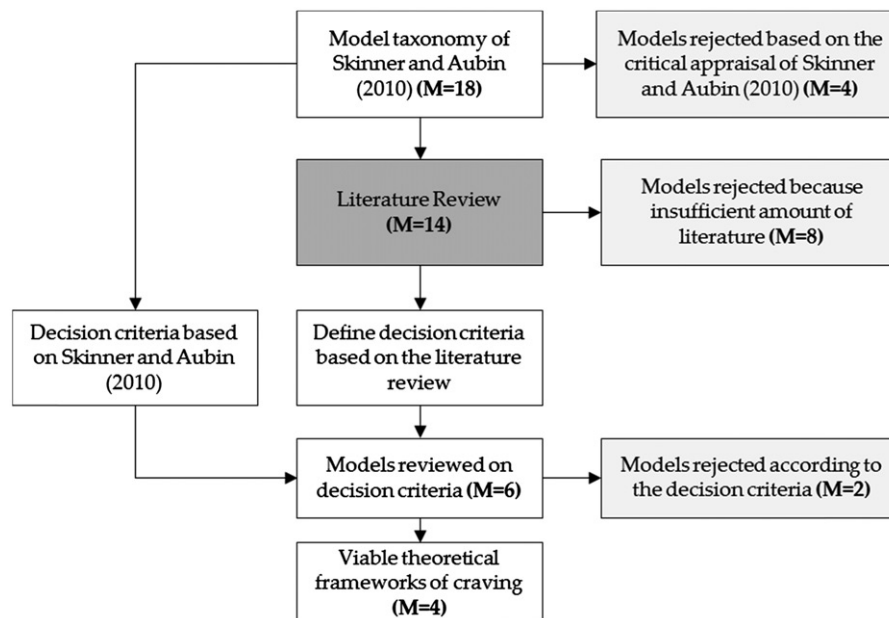


Figure 1. Schematic representation of the extraction of decision criteria. M represents the number of models included or excluded at each step of the procedure.

criteria: (1) performed animal or other nonhuman studies; (2) studies did not involve alcohol; and (3) non-English articles.

3. *Key term classification algorithm.* The key terms for each model were defined using an automated data-driven approach, with a key term classification algorithm. The key term classification algorithm was written with MATLAB 15 © (The MathWorks Inc., Natick, MA, 2000) and is available in the online supplementary materials. The key term classification algorithm extracts key

terms from the articles by searching through the titles and keyword fields (keyword fields as defined by articles' authors), resulting in a frequency table of single and combinations of words (keyterms) found for each model. The frequency tables can be requested from the authors.

4. *Removal of nondiscriminatory key terms.* As expected, the key terms with the highest numbers of articles were those that corresponded to the review context, namely: *craving*, *alcohol* and/or *urge*. However, these key terms



did not provide a relevant classification since all articles contained them. As all models are craving models, it is expected that all articles citing these models would have craving as keywords or title words. Non-useful key terms were those that pertained to: (1) conjunction/determiners (e.g. 'and'), (2) the context of the review (e.g. 'alcohol addiction'), (3) the subject of interest (i.e., 'craving'), and (4) a descriptors of statistical relations (e.g., 'correlation'). Several models did not have a key term occurring in at least four articles, indicating an insufficient number of homogenous articles to support these models. Subsequently, these models were not further included in this literature review.

5. *Full articles scanned on relevance.* The first author read the articles of the homogeneous groups and manually removed irrelevant articles, often due to an irrelevant target population. As the scope of this review is on the process of craving and relapse in persons with alcohol addiction, populations of for example social drinkers, often student samples, are considered not relevant for our purpose. After inferences are drawn for a specific model, an overall decision criterion based upon that single model inferences was defined in order to assess all models included in the review.

Figure 2 illustrates a flowchart of the literature search strategy.

#### Determining viable theoretical frameworks for alcohol craving research

The models were evaluated on the criteria from Skinner and Aubin (2010) and the literature review. The models and criteria obtained in the prior steps are presented in a tabular

format in the *Results* section. Models that in their assumptions violated at least one of the found criteria were rejected. From the remaining models that met the decision criteria, model parameters were selected and evaluated on their relevance for real-time and real world alcohol craving research.

#### Selecting parameters for real-time and real world craving research

Parameters were assessed as relevant when they fluctuated over short time periods, thus reflecting the episodic, and dynamic nature of substance use. Additionally, since craving is a construct primarily relevant within the context of attempts to sustain abstinence from drinking, the model parameters should be part of the process of craving and relapse rather than the process of substance use initiation or developing addiction. Furthermore, the parameters should allow clear operationalization in a natural environment.

#### Results

First, the findings from the literature review are presented. Second, an overview of the decision criteria obtained from all the sources is provided. Third, we present our decision for theoretical frameworks based on these criteria. Fourth, the selection of parameters from these theoretical frameworks relevant for real-time and real world craving research is presented.

#### Literature review

Table 2 shows the results of the literature search strategy. For the models that have no defined key terms in the last column, no relevant key term was found. These eight models

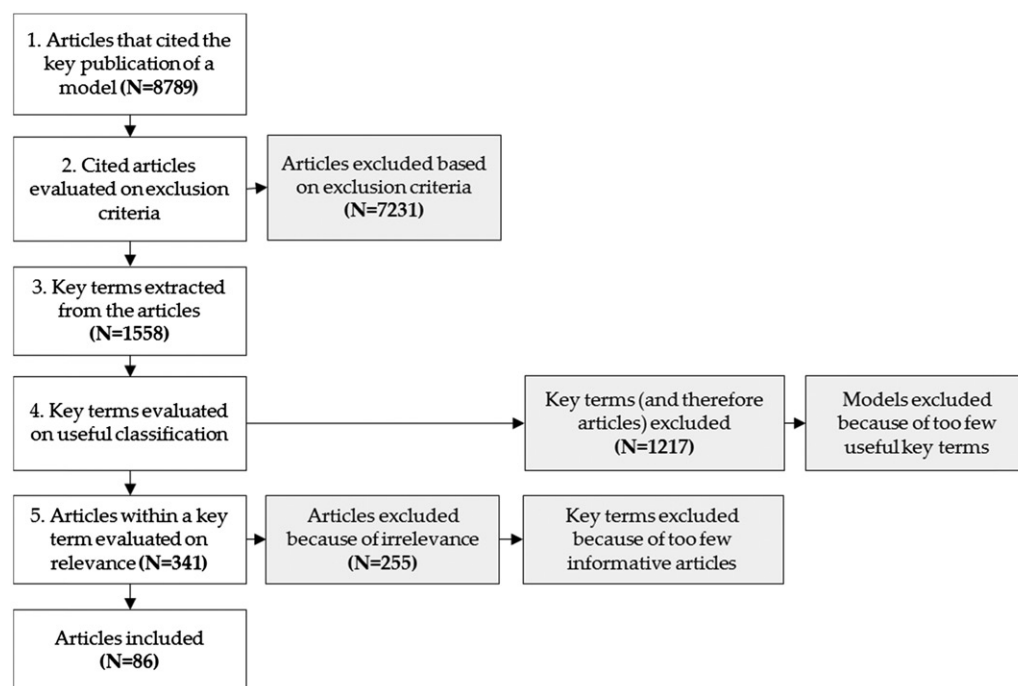


Figure 2. Flowchart of the literature search strategy. N represents the number of articles included or excluded at each step of the procedure.

**Table 2.** Results from snowballing and keyword extraction literature search strategy to identifying craving models. The first column shows the model with its founding publication. The second column shows the number of articles found with snowballing, and the third column shows the number of articles remaining after applying inclusion and exclusion criteria. The overview of key terms, the number of articles found on their basis, and the final number of relevant articles found are presented in the fourth column.

Models (founding publication)	Step 1. Number of articles found after snowballing the founding publication	Step 2. Number of articles after applying inclusion and exclusion criteria <sup>a</sup>	Step 3 & 4. Key word extraction <sup>b</sup> (Number articles found   Number articles relevant)
<b>Cognitive models</b>			
5. Outcome expectancy model* Marlatt (1985)	111	44	
6. Dual-affect model* Baker et al. (1986)	74	13	
7. Affective processing model of negative reinforcement Baker et al. (2004)	615	125	Negative affect (37 17)
8. Cognitive processing model Tiffany (1999)	1054	290	Attentional bias (34 20) Working memory (15 8)
<b>Psychobiological models</b>			
9. Three-pathway psychobiological model Verheul et al. (1999)	220	105	Reward (17 6) Withdrawal (9 4)
10. Incentive sensitization Robinson and Berridge (1993)	3890	331	Attentional bias (55 20)
11. Theory of neural opponent motivation Koob and Le Moal (1997)	1393	156	Stress (17 12)
12. Temporal-difference reinforcement learning model* Redish (2004)	216	15	
13. Unified framework for addiction* Redish et al (2008)	169	23	
14. Neuroanatomical model* Anton and Carolina (1999)	137	61	
15. Model of interceptive dysregulation* Paulus et al. (2009)	40	6	
<b>Motivational models</b>			
16. Motivational model of alcohol use Cox and Klinger (1988)	512	333	Drinking motives (157 20)
17. Multidimensional ambivalence model* Breiner et al. (1999)	68	37	
18. Prime theory* West and Hardy (2006)	290	19	

<sup>a</sup>The frequency tables were not included in the paper because of their length. These tables can be requested from the authors.

<sup>b</sup>Only the articles that have key terms in their title or author keywords are included. Models excluded are marked with an asterisk (\*).

were excluded since these were assumed not to have sufficient evidence for the purpose of this review. Note that for these models, only a small number of articles were found after inclusion and exclusion criteria were applied, confirming the limited empirical evidence available for these models. The remaining six models were further reviewed.

### Model 1. Affective processing model of negative reinforcement (Baker et al. 2004)

The affective processing model of negative reinforcement was cited by 125 articles, of which 38 contained the key terms ‘negative affect’ or ‘negative’ or ‘affect’. Articles with the key terms ‘negative’ and ‘affect’ were also separately screened to avoid excluding articles that, for example, addressed both *positive* and *negative affect* but merely used the key term *affect* instead. Of these 38 articles, 21 were excluded. This resulted in a total of 17 articles based on the affective processing model in which *negative affect* is addressed, as further described in the following sections.

#### Negative affect

Fifteen articles found that *negative affect* is an important predictor of drinking or relapse (Hussong 2007; Daughters et al. 2009; Spada & Wells 2009; Witkiewitz & Villarroel 2009; Simons et al. 2010; Witkiewitz & Bowen 2010; Cranford et al. 2011; Ostafin & Brooks 2011; Witkiewitz et al. 2011; Macpherson et al. 2012; McHugh et al. 2013; Schlauch et al. 2013; Simons et al. 2014; Treloar et al. 2015; Woud et al. 2015). Only two articles found that *negative affect* had no impact on relapse (Holt et al. 2012; Kabbani et al. 2014). Two studies found that higher positive affect – not negative affect – was associated with increased alcohol consumption (Peacock et al. 2015; Treloar et al. 2015). Only McHugh et al. (2013) found an effect of both *positive* and *negative affect*.

To conclude, given the strong evidence in favor of Baker and colleagues’ (Baker et al. 2004) model, *negative affect* is an important predictor of relapse. There are only some articles that find no relationship or that claim that *positive* and not *negative affect* is a relevant cause of relapse.

#### Conclusion

The model should incorporate *negative affect* as a predictor of relapse.

### Model 2. Cognitive processing model (Tiffany 1999)

For the cognitive processing model, the key concepts found in the literature with the key term extraction algorithm were: *attentional bias* and *working memory*. In our literature selection, *attentional bias* occurred in 34 of the 290 articles, of which 13 were excluded. Additionally, 15 articles contained the key term *working memory* of which seven articles were

excluded. Of the eight articles remaining, the findings were uninformative about the place and relevance of *working memory* in the process of craving, therefore, *work memory* was excluded in the review. The 20 articles relating to *attentional bias* are discussed below.

### **Attentional bias**

In the context of substance abuse, *attentional bias* refers to the observation that experienced alcohol users pay more attention to alcohol-related cues than neutral cues (Field et al. 2009). According to the cognitive processing model (Tiffany 1999), alcohol use is an automatic process, upon which patients have no influence. Therefore, high *attentional bias* towards alcohol cues compared to neutral cues in alcohol dependent subjects is expected.

In 12 articles, it was shown that dependent drinkers have a higher *attentional bias* towards alcohol cues than non-dependent controls (Carrigan et al. 2004; Dickter et al. 2014; Fadardi & Cox 2006, 2009; Fridrici et al. 2013; Garland et al. 2012a,b; Lusher et al. 2004; Noël et al. 2007; Sharma et al. 2001; Townshend & Duka 2001; Wilcockson & Pothos 2015). Only two studies found no or a negative difference between respondents who are alcohol dependent and respondents who are not (Ryan 2002; Townshend & Duka 2007).

Field et al. (2009) performed a meta-analysis of 68 independent data sets that together suggested a small but significant relationship between *attentional bias* and craving. In their review on *attentional bias* in addictive behaviors, Field and Cox (2008) concluded that *attentional bias* causes craving and vice versa. Cox et al. (2007) found that low *attentional bias* predicts alcohol reduction in excessive drinkers. Snelleman et al. (2015) found no prediction by *attentional bias* on relapse.

Three articles reviewed the effect of *attentional bias* retraining or alcohol attention control training. Schoenmakers et al. (2010) and Field et al. (2007) reported no effects of *attentional bias* retraining on craving nor relapse. Only alcohol attention control training (Fadardi & Cox 2009) led to a reduction of both *attentional bias* and alcohol consumption in harmful drinkers.

Although *attentional bias* occurs in dependent drinkers and may cause craving, there is less conclusive evidence that *attentional bias* predicts relapse or that modifying *attentional bias* contributes to recovery. The proposed automaticity of alcohol addiction according to the cognitive processing model still remains debatable.

### **Conclusion**

The model should explain that dependent drinkers have a higher *attentional bias* towards alcohol cues than nondependent drinkers.

### **Model 3. Three-pathway psychobiological model (Verheul et al. 1999)**

Two key terms were notably present: *reward* and *withdrawal*. Note that these represent the *reward* and *relief* pathways, but not the third obsessive pathway of the three-pathway model

(Verheul et al. 1999). Seventeen articles were found with the keyterm *reward*, from which 11 articles were excluded after scanning the full article. For the key term *withdrawal*, nine articles were found of which five were excluded because of irrelevance. The remaining four articles did not provide enough information to draw inferences on; therefore, *withdrawal* was excluded as keyterm.

### **Reward**

Heinz et al. (2003) found that drinking in positive emotional states contributes to *reward* craving. Two studies developed *relief* and *reward* craving test (Ooteman et al. 2006; Glöckner-Rist et al. 2013), where groups of *relief* and *reward* craving drinkers were both smaller than the remaining subjects which were defined as combination or no craving drinkers. Correspondingly, Grusser et al. (2006) found that problem drinkers showed a significantly higher amount of both *reward* and *relief* craving. Only Martinotti and colleagues (Martinotti et al. 2013) examined a questionnaire on all pathways of the model, namely *reward*, *relief* and *obsessive* craving. They confirmed that alcohol-dependent subjects had a higher mean score on all craving factors as compared to the normative sample.

To conclude, four studies found that the *reward* and *relief* pathways seem to occur either simultaneously or not at all in individual cases. Additionally, alcohol dependents seem to score higher than nondependent drinkers on the *reward*, *relief* and *compulsive* pathways of the model, not merely on *reward*. These findings are partly in line with the model, since the model claims that multiple pathways can occur simultaneously or be entirely absent. However, these conclusions are tentative due to the small number of studies upon which they are based.

### **Conclusion**

Inconclusive.

### **Model 4. Incentive sensitization theory of addiction (Robinson & Berridge 1993)**

For the incentive sensitization theory of addiction (Robinson & Berridge 1993), *attentional bias* was found to be a relevant key term in the literature. A total of 55 articles discussed *attentional bias*, of which 35 articles could be excluded due to irrelevance. Eleven articles overlapped the search on *attentional bias* of the cognitive processing model (Tiffany 1999). Nine of these articles mentioned both the cognitive processing and the incentive sensitization models when explaining the reasoning behind *attentional bias* (Townshend & Duka 2001; Lusher et al. 2004; Noël et al. 2007; Townshend & Duka 2007; Field et al. 2009; Garland et al. 2010; Schoenmakers et al. 2010; Dickter et al. 2014; Waters & Green 2003). The nine additional articles are reviewed below.

### **Attentional bias**

Of the nine articles, three showed that dependent drinkers have a higher *attentional bias* than the control group



(Waters & Green 2003; Miller & Fillmore 2011; Weafer & Fillmore 2012). Two of these studies (Miller & Fillmore 2011; Weafer & Fillmore 2012) looked additionally at the effect of alcohol intoxication on *attentional bias* and found that *attentional bias* decreases through alcohol drinking. This was in contrast to the findings of Schoenmakers et al. (2008) and Roberts et al. (2014), who found that low doses of alcohol increased *attentional bias*. Duka and Townshend (2004) found an increasing effect of *attentional bias* for a low alcohol dose and a decreasing effect on high doses of alcohol. This result differs from Schoenmakers and Wiers (2010) later findings and the findings of van den Wildenberg et al. (2006), where no significant effect of priming on *attentional bias* was found.

Multiple articles claim that *attentional bias* exists, as supported by both the cognitive processing model and the incentive sensitization theory of addiction. Furthermore, the incentive sensitization theory claims that repeated alcohol intake increases the automatized process. Multiple studies looked at the effect of alcohol priming, but the results were inconclusive. It is not clear from the model whether an increased *attentional bias* was expected immediately after priming. Therefore, no additional decision criterion was formulated.

### Conclusion

The model should explain that dependent drinkers have a higher *attentional bias* towards alcohol cues than nondependent drinkers.

### Model 5. Theory of neural opponent motivation (Koob & Le Moal 1997)

For the neural opponent motivation model, *stress* is an important concept as a predictor of relapse. The key term *stress* was found within 17 articles, and subsequently 12 of these articles were found relevant for this review.

### Stress

According to Fox et al. (2007), exposure to *stress* produced significant increases in alcohol craving, anxiety, and negative emotions. Ayer et al. (2011) found that daily *stress* predicts alcohol consumption and vice versa. Blomeyer et al. (2013) found that alcohol use increases with the number of stressful life events. Saraceno et al. (2009) performed a literature study and found that three studies reported a link between *stress* and problematic alcohol use and two studies suggested that individuals drink to regulate *negative affect* and to cope with negative life events.

Multiple studies found that alcohol-dependent subjects have a decreased physiological reaction to stressors (Lovallo 2011), as determined, for example, by measuring heart rate (Panknin et al. 2002; Brkic et al. 2015) or cortisol levels (Lovallo et al. 2000; Pratt & Davidson 2009; Nakajima et al. 2013). Lovallo (2006) argued that this decreased reaction may predict a high risk for future risky drugs and alcohol behavior. Nakajima et al. (2013) found that moderate alcohol

consumption was associated with an increased subjective response and altered hormonal sensitivity to *stress* in social drinkers who have the potential of becoming problem drinkers.

To conclude, *stress* seems to increase the risk of relapse. Additionally, multiple studies found a difference between alcoholics and healthy subjects on their *stress* response and baseline physiology. However, this particular finding is not suitable to formulate as decision criteria.

### Conclusion

The model should incorporate *stress* as a predictor of relapse.

### Model 6. Motivational model of alcohol use (Cox & Klinger 1988)

*Drinking motives* or *motives* were found as relevant key terms in 157 articles. A total of 137 articles were excluded after reading the full text, often because of irrelevant target populations. The remaining 20 articles are reviewed below.

### Drinking motives

Three studies looked at the difference between the positive and negative *motives* of dependent drinkers. Higher scores on negative reinforcement *motives* were found in dependent drinkers than in moderate drinkers (Mezquita et al. 2011) and such higher scores were found to be generally associated with drinking problems (Anderson et al. 2013). This effect on alcohol consumption of positive reinforcement *motives* was not found by Engels et al. (2005). Galen et al. (2001) found that *drinking motives* mediate the effects of both positive and negative expectations on alcohol use and alcohol-related problems.

Eleven articles reported on different *drinking motives* as defined by the motivational model of alcohol use (Cooper (1994)): enhancement, coping, social and conformity motives. Articles that found an effect of one of these motives on dependence or drinking are shown in Table 3.

Most of the studies related to *drinking motives* involved the different motivations defined by Cooper (1994). However, these are not directly relevant for the evaluation of the models' assumption, existing of motivation to drink. These studies do presume that alcoholics have motives to drink. However, it is always difficult to know whether this is a biased effect. When the researcher asks about specific *drinking motives*, respondents might feel that they are assumed to have *drinking motives* and, therefore, confabulate them. Consequently, it is not clear, based on these findings, whether drinking is motivated and, therefore, alcohol drinking is the individual's conscious decision. No decision criteria can be determined based on the studies presented.

### Conclusion

Inconclusive.

**Table 3.** Effect of drinking motives on dependence or drinking.

Motive	Articles that found an effect on dependence or drinking
Enhancement	Lyvers et al. 2010; Doyle et al. 2011; Hasking et al. 2011; Drerup et al. 2011; Kristjansson et al. 2011, 2012 <sup>o</sup> ; Glavak Tkalić et al. 2013; Piasecki et al. 2014; Cadigan et al. 2015*.
Coping	Agrawal et al. 2008; Beseler et al. 2008; Lyvers et al. 2010; Doyle et al. 2011; Littlefield et al. 2011 <sup>o</sup> ; Mackie et al. 2011; Mezquita et al. 2011; Kristjansson et al. 2011, 2012 <sup>o</sup> ; Fitzgerald and Long 2012; Gilson et al. 2013; Glavak Tkalić et al. 2013; Piasecki et al. 2014*; Rodriguez et al. 2014; Cadigan et al. 2015; Levitt and Leonard 2015.
Social	Agrawal et al. 2008; Beseler et al. 2008; Lyvers et al. 2010; Drerup et al. 2011; Mackie et al. 2011; Kristjansson et al. 2011; Mezquita et al. 2011; Gilson et al. 2013; Cadigan et al. 2015.
Conformity	Agrawal et al. 2008; Kristjansson et al. 2011; Fitzgerald and Long 2012.

<sup>o</sup>These studies are all on the same dataset. \*Effect on experiences outcomes.

### Decision criteria

As mentioned before, based on the review, decision criteria were derived from Skinner and Aubin's (2010) critical appraisal and the literature review. The following criteria were found in the literature review:

(1) The model should incorporate *negative affect* as a predictor of relapse. (Affective processing model of negative reinforcement)

(2) The model should explain that dependent drinkers have a higher *attentional bias* towards alcohol cues than nondependent drinkers. (Cognitive processing and Incentive sensitization model)

(3) The model should incorporate *stress* as an increased risk of relapse. (Theory of neural opponent motivation)

In addition to decision criteria based on the literature, decision criteria were also retrieved from Skinner and Aubin's (2010) critical assessment of models (as summarized in Table 1). As the literature search strategy yielded six of these models to be included in the final review, only their criticisms regarding these models were included as decision criteria. This generated the following additional criteria:

(4) The model explains why people experience craving and relapse, sometimes even after long periods of abstaining. (Affective processing model of negative reinforcement, (Skinner & Aubin 2010, p. 611))

(5) The model should explain irrational/compulsive side of craving is. (Motivational Model, (Skinner & Aubin 2010, p. 618))

(6) The model should explain how craving can occur without consumption or how consumption occurs without craving. (Three-pathway psychobiological model, (Skinner & Aubin 2010, p. 614))

For the affective processing model of negative reinforcement, Skinner and Aubin (2010) also formulated the criticism that the relief of aversive withdrawal symptoms cannot be an important determinant of addiction because some drugs are highly addictive without producing highly unpleasant syndromes (p. 613). However, this criterion was not included as it is not accurate for alcohol addiction.

### Determining viable theoretical frameworks for alcohol craving

Based on these criteria the viability of the six remaining models was assessed. Table 4 shows how the models are evaluated on the six decision criteria defined in the previous steps. Only the critical findings for each of the six included models are described next. When a model suffices on a criterion this is not separately discussed and can be found in the table.

The affective processing model of negative reinforcement (Baker et al. 2004) claims that *attentional bias* occurs, because the organism focuses on the response option (i.e., drug use) that is associated with quick and efficient control next to relief of negative affect. Whether this bias is the same *attentional bias* found in the empirical studies in this review is unclear, since no articles reviewed the effect of negative affect on *attentional bias*. However, the model does not seem to pose a contradiction to this decision criterion. The only other critique is the weak justification of craving and relapse after long periods of abstaining. Since the model does not violate either criteria, the model is included as theoretical framework.

The cognitive processing model (Tiffany 1999) claims that drinking is an automatized process and not an alleviation of *negative affect* and *stress*, as found in the literature review. Tiffany (1990) argues that alcohol cues from the environment, the emotional network or the time of the day, trigger this automatized process. *Negative affect* and *stress* could be triggers from the emotional network; however, this is merely interpretation. Tiffany (1999) claims that drinking is an automated process, which can be blocked when an individual chooses to abstain, which subsequently causes craving. However, it is not clear why a person does chooses not to abstain, but 'chooses' alcohol above other important things in life (e.g. having work, friendships). However, since the model does not violate the criteria explicitly, this model is included as theoretical framework.

The literature review showed that empirical evidence only supports the *relief* (decision criterion 1) and *obsessive* (decision criterion 5) of the three pathways model. This could be an artifact of the focus in this review on addicted individuals as the target population. For example, the *reward* path defined by the model could be evident in social drinkers, but not in dependent drinkers. Additionally, the model does not explain why people relapse without experiencing craving or why they experience craving and relapse after long periods of abstaining. More importantly, though, is the lack of validation of the pathways. The *obsessive* path was only investigated by one study (Martinotti et al. 2013). Other studies related merely focused on the *relief* and *reward* pathways, showing that participants experience either both craving paths or none of the paths (Grusser et al. 2006; Ooteman et al. 2006; Glöckner-Rist et al. 2013). Although the authors propose that individuals can indeed experience all or none of the craving paths, the apparent lack of studies showing any differentiation between paths indicates this core assumption of having different pathways to be invalid and the model is therefore rejected.

**Table 4.** Results for each model on the decision criteria in order to determine the most suitable model.

Affective processing model of negative reinforcement (Baker et al. 2004)	Cognitive processing model (Tiffany 1999)	Three-pathway psychological Model (Verheul et al. 1999)	Incentive sensitization (Robinson & Berridge 1993)	Theory of neural opponent motivation (Koob & Le Moal 1997)	Motivational model of alcohol use (Cox & Klinger 1988)
<p><b>1. The model should incorporate negative affect as a predictor of relapse.</b></p> <p><b>Yes:</b> The negative affect model acknowledges this as the most prominent predictor of the relapse process. Baker et al. (2004) see negative affect as a withdrawal signal, meaning that next to tremors or extensively sweating, a person in rehabilitation experiences fear, depression and other negative affect symptoms.</p>	<p><b>Unclear:</b> The cognitive processing model does not specify negative affect as specific cue for relapse. Tiffany (1999) mentions that cues can come forward from a person's emotional state, possibly including negative affect.</p>	<p><b>Yes:</b> The three-pathway model mentions both positive and negative affect as equally relevant predictors. This model is therefore either partly incorrect according to the review or partly irrelevant for a system where dependent drinkers are the target population.</p>	<p><b>No:</b> The incentive sensitization model states that a person starts drinking for positive reasons, but because of repeated drug intake an incentive sensitization process is activated, leading to compulsive craving. (Robinson and Berridge 1993) mention stress as a possible initiator of a relapse process.</p>	<p><b>Yes:</b> The theory of neural opponent motivation has negative affect as important reason of relapse. Negative affect is seen as a withdrawal effect.</p>	<p><b>Yes:</b> One important motivation in the motivational model is to avert negative situations. However, another equally important motivation is to enhance a positive situation.</p>
<p><b>2. The model should explain that dependent drinkers have a higher attentional bias towards alcohol cues than nondependent drinkers.</b></p> <p><b>Yes:</b> The negative affect model argues that if there is no immediate relief from distress, the individual is biased towards response options (alcohol use) that most effectively have alleviated negative affect in the past. Whether this bias is the same attentional bias found in the empirical studies from this review is debatable, however the model does not seem to pose a contradiction to the finding of attentional bias.</p>	<p><b>Yes:</b> The cognitive processing and incentive sensitization model are often mentioned as explanations for the attentional bias effects in a Stroop task. The cognitive processing model accounts for attentional bias; but it remains unclear whether attentional bias gives foundation to the cognitive processing model.</p>	<p><b>Unclear:</b> Verheul et al. (1999) give no explicit explanation for attentional bias. However, when assumed that attentional bias explains compulsive addiction, then the three-pathway model has support for the compulsive path of the model.</p>	<p><b>Yes:</b> Attentional bias is explained in the model. However, it is unclear whether attentional bias gives foundation to the incentive sensitization model.</p>	<p><b>Unclear:</b> Koob and Le Moal (1997) indicate that the process of wanting (as they call craving) is compulsive, but whether this causes attentional bias is unclear.</p>	<p><b>Unclear:</b> Cox and Klinger (1988) give no explicit explanation for attentional bias.</p>
<p><b>3. The model should incorporate stress as an increased risk of relapse.</b></p> <p><b>Yes:</b> Stress is an important predictor of negative affect according to the affective processing model of negative affect.</p>	<p><b>Unclear:</b> Stress could be a cue for the relapse process coming from a person's emotional network. However this is not specified.</p>	<p><b>Yes:</b> Stress is the initiator of the second pathway called need for relief, leading to a motive for drinking.</p>	<p><b>Yes:</b> Robinson and Berridge (1993) claim that stress activates a similar process as alcohol priming, increasing the chance on relapse.</p>	<p><b>Yes:</b> Stress is a trigger of relapse.</p>	<p><b>Unclear:</b> Stress is not explicitly mentioned.</p>

(continued)

**Table 4.** Continued

Affective reinforcement model of (Baker et al. 2004)	Cognitive processing model (Tiffany 1999)	Three-pathway psychobiological Model (Verheul et al. 1999)	Incentive sensitization (Robinson & Berridge 1993)	Theory of neural opponent motivation (Koob & Le Moal 1997)	Motivational model of alcohol use (Cox & Klinger 1988)
<p><b>4. The model explains why some people experience craving and relapse even after long periods of abstaining.</b>  <b>Partly:</b> This is the major argument against this model according to Skinner and Aubin (2010) because it is entirely built around the idea of withdrawal affect. Baker et al. (2004) claim that withdrawal symptoms are more prolonged than once thought.</p>	<p><b>Yes:</b> The cognitive processing model explains that feelings of craving after long abstinence can be caused by a configuration of cues that can trigger a person back into automatic consumption. This only happens on some very specific and rare occasions.</p>	<p><b>Yes:</b> Verheul et al. (1999) do not explain this.</p>	<p><b>Yes:</b> Robinson and Berridge (1993) claim that the brain of an addicted individual is permanently altered, making them always vulnerable.</p>	<p><b>Yes:</b> The brain of an addicted individual is permanently altered, making them always vulnerable.</p>	<p><b>Unclear:</b> Cox and Klinger (1988) do not explicitly explain why people relapse after long periods of time. Maybe relapse is due to the change in the individual's current situation expectations of what drinking might change in the situation.</p>
<p><b>5. The irrational/compulsive side of craving is explained by the model.</b>  <b>Unclear:</b> Tiffany (1990) claims that the process of drinking is automatized, and might therefore be claimed to be compulsive. However, when somebody is abstaining this person forms a blockage in this automatized process, which leads the craving. It is not explained why people choose to drink compulsively above everything else.</p>	<p><b>Yes:</b> The three-pathway psychobiological model has a compulsive pathway as one of its three pathways.</p>	<p><b>Yes:</b> Sensitization is the process of giving a higher incentive to alcohol every time alcohol is consumed. This concept infers that alcohol is perceived to have a high reward over a period of time, which explains the irrational/compulsive side of craving.</p>	<p><b>Yes:</b> The irrational side is explained by sensitization and counter adaptation.</p>	<p><b>No:</b> The motivational model claims that drinking is always a motivated choice and, as such, ignores the irrational side of craving. This is generally seen as an unacceptable deficiency of this model.</p>	<p><b>Yes:</b> Choice is always a mediating variable, meaning that a person always makes a rational choice whether or not to drink. This idea implies that craving triggers a rational decision process, not always leading to relapse.</p>
<p><b>6. The model should explain how craving can occur without consumption or how consumption occurs without craving.</b>  <b>Yes:</b> Baker et al. (2004) claim that negative affect is highly determinant of relapse. However, this process may occur without craving.</p>	<p><b>Yes:</b> The cognitive processing model assumes that addicts drink automatically, without experiencing craving. Only when this automatic process is blocked, does craving occur (which would not always lead to consuming).</p>	<p><b>No:</b> Craving is assumed to cause relapse. This is the critique of this model.</p>	<p><b>No:</b> Craving (wanting) is assumed to cause relapse.</p>	<p><b>No:</b> Craving (wanting) is assumed to cause relapse.</p>	<p><b>Yes:</b> Choice is always a mediating variable, meaning that a person always makes a rational choice whether or not to drink. This idea implies that craving triggers a rational decision process, not always leading to relapse.</p>



**Table 5.** Parameter selection from the different models in the theoretical frameworks defined.

Affective processing model of negative reinforcement (Baker et al. 2004)	Cognitive processing model (Tiffany 1999)	Incentive sensitization (Robinson & Berridge 1993)	Theory of neural opponent motivation (Koob & Le Moal 1997)
<b>1. The parameters describe the continuous and cyclical process of craving and relapse in an enduring addiction, rather than the process of developing an addiction.</b>			
<b>Yes:</b> The negative affect model is predominantly about the process of relapse.	<b>Yes:</b> The cognitive processing model merely describes the process of being addicted.	<b>Both:</b> The main focus of the model is about becoming addicted and not about the process of relapse. However, it also gives some triggers for the relapse process.	<b>Both:</b> The theory of neural opponent motivation describes both the processes of becoming and being addicted.
<b>2. The parameters are episodic states that fluctuate over time.</b>			
<b>Yes:</b> Baker et al. (2004) state that negative affect grows over time, leading to an increase of craving.	<b>Yes:</b> The cognitive processing model assumes that cues are triggers for the automated drinking process. These triggers are not always present and, therefore, differ over time.	<b>Yes:</b> The incentive sensitization model assumes that alcohol receives a higher incentive by drinking. This incentive value grows over time.	<b>Yes:</b> According to Koob and Le Moal (1997) a first self-regulation failure leads to emotional distress and negative affect which causes relapse.
<b>3. The parameters can be operationalized in a natural environment.</b>			
<b>Yes:</b> The negative affect suggests negative affect, stress and as parameters.	<b>Unclear:</b> The cognitive processing model describes that multiple processes can be automatized and therefore 'trigger' drinking behavior. However, Tiffany (1999) is not specific about what these are. Arguably, these may differ between subjects. However, this also complicates translation into generic monitoring parameters.	<b>Yes:</b> According to the incentive sensitization model triggers are can be operationalized into stress and priming by alcohol or other drugs.	<b>Yes:</b> The model can be operationalized into stress and negative affect.

For the incentive sensitization theory of addiction (Robinson & Berridge 1993), only the *attentional bias* experiments provided support. It is evident that *attentional bias* towards alcohol cues exist in dependent drinkers. However, it is not clear from the fact that it is present in dependent drinkers, what the role is of this *attentional bias* in the process of craving (Christiansen et al. 2015). It is therefore questionable whether *attentional bias* provides viable evidence for the model. Additionally, *attentional bias* only yielded small effect on craving and no effect on relapse. The model does not explain why craving is not always followed by relapse. Furthermore, when describing this process of relapse, Robinson and Berridge (1993) mention *stress* and *priming* as predictors of relapse and not *negative affect*. Concluding, the case could be made that the model is incomplete rather than invalid and therefore the model is included as part of the theoretical frameworks.

The theory of neural opponent motivation (Koob & Le Moal 1997) is a neural model based primarily on research with animals, whereas this review was limited to human research. However, enough studies with a human sample were found to evaluate the model. Koob and Le Moal (1997) give no explicit explanation of *attentional bias*. An additional limitation of the model seems to be that it is not explained how relapse could occur without craving. However, these two limitations expose rather an incomplete model than an invalid one, leading to the inclusion of this model as theoretical framework.

The motivational model claimed that drinking is always a motivated choice. The motivational model Averting *negative affect* situations is one of the motivation for drinking. However, *stress* and *attentional bias* are not explicitly explained. Additionally, Skinner and Aubin (2010) effectively

argued that this model ignores the irrational side of craving. Moreover, no sufficient evidence for deliberate decision making was found and as a result this model is currently rejected. Further research should be focused on substantiating this motivated choice.

Summarizing, the affective processing model of negative reinforcement (Baker et al. 2004), the incentive sensitization theory of addiction (Robinson & Berridge 1993), cognitive processing model (Tiffany 1999) and the theory of neural opponent motivation (Koob and Le Moal 1997) are determined to be (partly) relevant as viable theoretical frameworks.

### Selecting parameters for real-time and real world craving research

In this final step, parameters are retrieved from the theoretical framework determined in the previous section. As we stated previously, the parameter should be suitable for real-time monitoring, implying that the parameters should:

1. describe the continuous and cyclical process of craving and relapse in an enduring addiction, rather than the process of developing an addiction.
2. be an episodic state that fluctuates over time.
3. be operationalizable in a natural environment.

Table 5 shows how the models are evaluated for parameter selection to fit the real-time and real world focus of this review.

With regard to the first two criteria, parameters from all four models appear suitable. The cognitive processing model and the affective processing model of negative reinforcement describe the process of relapse rather than the development



of addiction, as preferred in this review. The incentive sensitization model and the theory of neural opponent motivation explain both the process of relapse and the development of addiction. All four models incorporate parameters that fluctuate over time. The specific time varying parameters can be found in Table 5.

With regard to the third criterion, operationalizability in a real world setting, from three models potentially suitable parameters emerge. The affective processing model of negative reinforcement (Baker et al. 2004) suggests *negative affect* and *stress* as parameters. *Negative affect* and *stress* are already used in some real-time and real world studies, for multiple examples see Serre et al. (2015). For the cognitive processing model, Tiffany (1990) argues that *alcohol cues* from the environment, the emotional network or the time of the day, trigger the automatized process. The nature of the triggers is described in a rather general way and the translation to concrete cues seem to be dependent on the individual. In the articles included in the review neither clear operationalizations of these cues were formulated, nor was the predictive value of such cues on the automatized process studied. Therefore, additional research is warranted to prevent arbitrary selection of specific cues. The incentive sensitization theory of addiction (Robinson & Berridge 1993) would lead to *stress* and *priming by alcohol or other drugs* as parameters. However, since *priming* is difficult to operationalize in a natural context and is not supported by empirical evidence within this review, it is not selected as relevant parameter. The theory of neural opponent motivation (Koob & Le Moal 1997) also proposes *stress* and *negative affect* as relevant parameters, but adds no other explicit parameters in line with the focus on real-time and real world research. Additionally, *attentional bias*, since emerging from this review, could be deemed a relevant parameter for the cognitive processing model and incentive sensitization theory of addiction. However in the case of attentional bias, two issues remain. First, although it is suggested that *attentional bias* is an output of the underlying automated process at a moment in time, evidence to support this hypothesis is lacking. Second, *attentional bias* is found to have only a small effect on craving (Field 2009) and no convincing evidence for a causal influence on relapse is found, in agreement with a meta-analysis of Christiansen et al. (2015). Christiansen et al. (2015) propose that future research should use experience sampling methodology to assess the clinical significance of fluctuations in *attentional bias* over time. However, currently it is not a parameter supported by evidence.

## Discussion

The aim of the present study was to identify viable theoretical frameworks of craving as the first step towards selecting essential parameters for real-time alcohol craving research. The results of this review show that *negative affect* and *stress* are relevant parameters, since the three craving models with sufficient empirical foundations support these. Below, we further discuss our findings, offer suggestions on how to use the finding in real-time and real world craving research and

argue as to where our results or research methodology could be of further use in current research fields.

In this review, six empirically supported models from all three domains (cognitive, psychobiological, and motivational models) emerged that contribute to our understanding of craving and relapse in alcohol addiction. Based on these six models, three key terms with robust evidence appear to be *stress*, *negative affect* and *attentional bias*. Additionally, for *drinking motives*, *reward*, *relief*, *withdrawal* and *working memory* limited support was found. When restricting the evidence to the focus on ecological monitoring, *stress* and *negative affect* clearly remain as viable constructs. *Attentional bias*, although found as a possible predictor of craving, is not proposed as a parameter in the framework since it has not shown to be predictive of relapse. Two parameters found within the viable models without empirical support were *alcohol cues* and *priming*. Although *alcohol cues* have been shown relevant triggers for craving in a lab setting, often using exposure to alcohol related pictures, this concept lacks ecological validation as well as standardized operationalization procedures in an ecological context (Carter & Tiffany 2001). Similarly, *priming* seems difficult to operationalize in a natural context, and was also not supported by sufficient empirical evidence within this review. Concluding, in addition to *stress* and *negative affect* the parameter *alcohol cues* could be included for lab experiments, and when focusing solely on relatively stable conditions of dependent drinkers attentional bias is a well proven concept.

The findings of this review, and in particular the identified theoretical frameworks and corresponding parameters for craving, could be useful in studying high-risk negative affect and stress situations with increased chances of relapsing. As suggested by Rohsenow and Monti (1999), creating awareness of and especially prompting individuals to activate their coping skills in these high-risk situations might lower the chances of relapse. However, in order to timely detect high-risk *negative affect* and *stress* situations, continuous measurement of the fluctuating parameters is needed. Baker (in: Shaw 2006) recommends using biomonitoring (with wearables) to detect stressful events, since individuals may actually be unaware of upcoming stress or negative moods. Shaw (2006) then explains that heightened skin conductance, heart pulse rate and muscle tension, usually accompany higher states of arousal, and that these physiological indicators can be measured by wearable technology available today. We propose therefore that there might be a benefit of creating awareness and prompting individuals based on physiological responses instead of assuming that a person self will be always aware of underlying negative affect and stress. This implies that, physiological measurements of psychological events has added potential to detect high-risk situations early and prevent relapse by alarming an individual prior to the affective peak of the event.

Notably, this review also illustrates the dearth of evidence, both on the level of models, as with regard to single parameters within models. For twelve models insufficient (alcohol related) human studies were retrieved to make any inferences. For the six remaining models with empirical support, no more than a single key term emerged per model,

implying that multiple other concepts still need to be explored for full model validation. In fact, this review showed that research directly validating foundations and assumptions of craving models remains limited, as was already mentioned by Drummond in 2001. We found that, although most craving researchers do justify their study design and rationale with one or more model, an explicit attempt to discuss the theoretical implications of their findings is often lacking or neglected. Apparently, theories are primarily applied deductively, while the inductive loop from observations back to theory is largely overlooked. In sum, this calls for more studies validating theory, and for scholars to discuss in more depth the implications of their studies on the theories used. In fact, this review showed that the research on the foundations and assumptions of craving models remains limited.

We specifically developed the present review method for the purposes of determining viable theoretical frameworks, without having to perform a full meta-analysis for every model or every relationship within each model. In this, we relied on the scrutiny within the scientific community to cite the founding article of each model. Aside from otherwise being practically infeasible, this would probably have turned out unproductive as well, as multiple models are descriptive in nature, rather than having a clear predictive factor structure. The review methodology presented in this paper could potentially be useful for multiple other purposes in which there is a similar need to feasibly condense such a large quantity of evidence. The only prerequisite would be possessing founding publications that would allow a snowballing search approach. The method has shown to be a promising way to efficiently arrive at relevant theoretical frameworks within a complex, multidisciplinary field.

Finally, even though the models are denoted as craving theories by Skinner and Aubin (2010) no empirical findings in this review show the essential position of craving in the process of relapse. Several explanations for this finding are conceivable. First, the large majority of studies employ relapse or alcohol problems as dependent variable, rather than craving, which in turn might indicate a difficulty in operationalizing craving. Second, many studies may have included analyzes on craving, however found no significant results. Meaning that as in any review the risk of a publication bias (Ioannidis 2005) may also have occurred in this review. Third, assuming that the first explanation would be falsified, this lack of evidence regarding the concept of craving may actually reflect the non-viable nature of this construct. However, we tend to agree with Drummond (2001) who argues that it seems premature to dismiss the relevance craving, prior to consensus in the appropriate method to measure craving. Particularly he mentions that first more must be known about the human craving experience in the natural drinking environment.

## Conclusions

In this review, the affective processing model of negative reinforcement (Baker et al. 2004), the cognitive processing model (Tiffany 1999), the incentive sensitization theory of

addiction (Robinson & Berridge 1993) and the theory of neural opponent motivation (Koob & Le Moal 1997) were determined to be relevant for viable theoretical frameworks, leading to *negative affect* and *stress* as relevant parameters to include in real-time, real world alcohol craving research. *Attentional bias*, although found as a possible predictor of craving, is not proposed as a parameter in the framework since it has not shown to be predictive of relapse. Similarly, *alcohol cues* could be relevant triggers for craving, however this concept needs further operationalization and empirical foundation. Ultimately, we indicate that *negative affect* and *stress* emerge as the most promising parameters to include in real-time ecological craving research.

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