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Eye tracking correlates of acute alcohol consumption: A systematic and critical review

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Highlights

- We review studies using eye tracking measures in acute alcohol intoxication
- Studies focused on perception, attention, memory/executive functions and prevention
- We identify the limits of available data and describe new research avenues
- Guidelines are proposed, notably for alcohol consumption and eye tracking measures

Abstract

Eye tracking has emerged as a reliable neuroscience tool indexing the eye movements' correlates of impairments resulting from alcohol-use disorders, ranging from perceptive abilities to high-level cognitive functions. This systematic review, following PRISMA

guidelines, encompasses all human studies using eye tracking in participants presenting acute alcohol consumption. A literature search was conducted in PsycINFO, PubMed and Scopus, and a standardized methodological quality assessment was performed. Eye tracking studies were classified according to the processes measured (perception, attentional bias, memory, executive functions, prevention message processing). Eye tracking data centrally showed a global visuo-motor impairment (related to reduced cerebellar functioning) following alcohol intoxication, together with reduced memory and inhibitory control of eye movements. Conversely, the impact of such intoxication on alcohol-related attentional bias is still debated. The limits of this literature have been identified, leading to the emergence of new research avenues to increase the understanding of eye movements during alcohol intoxication, and to the proposal of guidelines for future research.

Keywords

Eye tracking; alcohol; acute alcohol consumption; saccade; dwell time

1. Introduction

Alcohol-related behaviors comprise a broad range of disorders that all may significantly contribute to various physical and mental health damages (WHO, 2018). Beyond the largely explored cognitive and brain consequences of chronic (e.g., Bühler & Mann, 2011, Stavro et al., 2013) or episodic (e.g., Carbia et al., 2018; Hermens et al., 2013) excessive alcohol consumption, the deleterious

effects associated with acute alcohol consumption have been the focus of many scientific works in the last decades. At the pharmacological level, two of the key primary targets of alcohol are NMDA and GABA_A receptors (e.g., Most et al., 2014; Spanagel, 2009). The initial modifications related to these systems generate a cascade of effects on a large range of neurotransmitters, including monoamines, opioids and endocannabinoids. These indirect effects are centrally involved in the reinforcing properties of alcohol, and in fine in the development of alcohol-related disorders (Vengeliene et al., 2008). Alcohol intoxication thus simultaneously reduces the excitatory responses of NMDA receptors (Lovinger et al., 1989; Nevo & Hamon, 1995) and conversely increases the inhibitory response of GABA_A receptors (Lobo & Harris, 2008; Santhakumar et al., 2007). This combined NMDA antagonism and GABA agonism causes a disequilibrium in the excitatory/inhibitory balance of the brain, resulting in a globally reduced central nervous system's activity. Such neurobiological modifications following acute alcohol consumption are thus associated with large-scale modifications of brain functioning, which have been largely described by electrophysiological or neuroimaging studies. These works have centrally reported reduced (in cerebellar/frontal areas) or exacerbated (in ventral tegmental area and nucleus accumbens, as a consequence of the reduced inhibitory influence of frontal regions on reward system) brain activations following acute consumption (Bjork & Gilman, 2014). The final behavioral output of these neurobiological and neurofunctional changes induced by alcohol intoxication is the impairment of various cognitive abilities due to globally reduced brain functioning. Indeed, many psychological and neuropsychological studies have reported that alcohol intoxication is related to a wide range of deficits encompassing visuo-motor (e.g., Poulsen et al., 2007), attentional (e.g., Nikolaou et al., 2013), memory (e.g., Wetherill & Fromme, 2011), inhibition (e.g., Field et al., 2010), higher-order executive (e.g., Spinola et al., 2017) or emotional (e.g., Capito et al., 2017)

processes (see Zoethout et al., 2011 for a review). Beyond this negative impact on cognitive abilities, acute alcohol consumption is also thought to boost the salience of alcohol cues, through the exacerbated activation of the reward system. This ends up in increased craving and alcohol-related cognitive biases (e.g., Field & Cox, 2008).

These neuropharmacological, neuroscience and neuropsychological data have recently been complemented through insights offered by other methods, among which eye tracking measures. This technique, by notably allowing the automatic detection of eye position and gaze direction with a high temporal resolution, is a useful mean to link the behavior and the underlying brain mechanisms. Indeed, the eye movements observed during cognitive tasks constitute a reliable index of the underlying psychological processes involved, and of the functioning of the brain regions related to each process (Luna et al., 2008). A classic example of these connections between eye movements and cognitive functions is offered by the numerous studies using saccadic eye movements measures to explore a large range of neuropsychological abilities. While they might at first sight appear quite automatic and independent from cognitive abilities, eye saccades are actually influenced by attentional, memory and executive processes, and involve a distributed cerebral network including both subcortical (striatum, thalamus, superior colliculus, and cerebellum) and cortical (primary visual, extrastriate, and parietal cortices, as well as frontal and supplementary eye fields) structures (McDowell et al., 2008). Fine-grained paradigms have thus been developed during the last decades to use saccadic eye movements as a way to evaluate these high-level cognitive functions, and to deepen their understanding beyond behavioral or neuroscience techniques (see Hutton, 2008 for a review). But the use of eye tracking to assess cognition goes far beyond saccadic measures, as several parameters can be measured through eye tracking (e.g., smooth-pursuit movements, pupillary diameter, fixation times, Lisberger, 2010), each being

relevant to explore specific cognitive processes, from basic visual perception (e.g., visual acuity), to attention, memory and learning or executive functions (Eckstein et al., 2017; Jones et al., 2014; König et al., 2016; Lai et al., 2012; Popa et al., 2015; Theeuwes et al., 2009). More specifically, the duration, speed and amplitude of eye movements are usually tracked to assess low-level visuomotor abilities (e.g., Leigh & Kennard, 2004). Attentional processes can be indexed by measuring the ability to efficiently modify gaze position and foveal focus according to goal-directed (voluntary) or stimulus-driven (involuntary) changes, as these eye movements reflect the reorientation of attentional resources (Deubel & Schneider, 1996). In the same line, long-term memory encoding can be investigated by analyzing the scanpaths of participants watching pictures which details have to be memorized (Harvey et al., 2013a), and spatial working memory can be assessed with a task in which participants have to make saccades towards the locations of previously presented targets (Paolozza et al., 2014). Regarding executive functions, inhibition is typically assessed using the antisaccade task, where participants have to perform saccades in the opposite direction of a target occurring on the screen, and thus to inhibit the reflexive saccade towards the target (Munoz & Everling, 2004).

Beyond their extensive usefulness to renew the knowledge on cognitive functioning in healthy populations, eye tracking tools can also be of high interest to measure the impairments associated with acute alcohol consumption, as alcohol intoxication strongly impairs visual processing and its related cognitive functions. Indeed, at the peripheral level, alcohol intoxication negatively impacts the functioning of most eye structures, including crystalline lens and retina (e.g., Wang et al., 2008; Xu et al., 2009). It has also been found that alcohol generates impairments in eye functioning (e.g., nystagmus; Mulvihill et al., 2007). At the brain level, the above-mentioned impact of acute alcohol consumption on the excitatory/inhibitory neurotransmission balance affects the brain regions

involved in visual processes: Alcohol intoxication centrally reduces cerebellar activity (e.g., Quinet & Goffart, 2015), alters cranial nerves functioning (Peragallo et al., 2013) as well as motor and visual brain areas (Bülher & Mann, 2011), resulting in a massive deleterious effect on eye movements. These impairments are further reinforced by the above-mentioned impact of alcohol intoxication on the attentional, memory and executive processes underlying eye movements, their exploration thus constituting an ideal way to obtain a comprehensive view of the behavioral and cerebral consequences of acute alcohol consumption.

As eye tracking efficiently complements the behavioral and neuroscience measures of a large range of cognitive processes (from basic perceptive abilities to high-level functions), and as a large range of eye movements are impaired following alcohol intoxication, eye tracking measurement constitutes an innovative tool to deepen our understanding of the deficits generated by alcohol intoxication. Several studies have applied this technique to populations with acute alcohol intakes, but these results are very scattered in terms of alcohol administration procedure, explored cognitive processes and used eye tracking indexes, and no comprehensive and systematic review has been proposed on this topic. The main aim of the present paper was thus to review all the studies which offered insights on alcohol intoxication through the use of valid eye tracking measures.

2. Methods

2.1. Research question, articles identification and selection procedure

Our research question was specified through the PICOS procedure (Population, Intervention, Comparator, Outcome, Setting; Liberati et al., 2009). Regarding the population, we considered studies in which human participants were administered alcohol and/or in

which acute alcohol consumption was evaluated. Concerning intervention/exposure, the review was limited to studies which included a reliable measure of acute alcohol exposure. For what pertains to the comparator, studies were considered if they offered a reliable comparison between an experimental group confronted with alcohol exposure and a matched control group. The outcome was focused on studies which proposed at least one reliable eye tracking measure (i.e. initial fixation, number/time of saccades, eye movements, gaze direction, dwell time, pupillary measure) as a dependent variable. Finally, regarding the setting, we included studies related to any type of design based on comparisons between groups or experimental conditions (i.e. interventional, observational, cross-sectional), thus excluding single-case or case series studies, as well as papers not reporting experimental data (i.e. review, meta-analysis, reply, commentary, erratum, conference proceedings).

This systematic review was conducted following the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), and we adhered to their 27-item checklist (Moher et al., 2009). Three databases were consulted (PsycINFO, Pubmed and Scopus). We focused on peer-reviewed articles published in English, between 1st of January 2000 and 10th of September 2018. The search phrase combined eye tracking words ("eye tracking" OR "eye-tracking" OR "eye movements" OR "visual tracking" OR "gaze tracking") and an initially large range of alcohol-related terms, in order to include all alcohol-related studies that might propose a measure of alcohol intoxication ("alcoholism" OR "alcohol dependence" OR "alcohol use disorder" OR "binge drink*" OR "heavy drink*" OR "social drink*" OR "episodic drink*" OR "college drink*" OR "alcohol*" OR "acute alcohol consumption" OR "fetal alcohol syndrome" OR "fetal alcohol disorder"). The initial search led to identify 995 papers (325 in PsycINFO, 227 in Pubmed, 443 in Scopus). The papers to be included in the review were then selected according to a 3-step procedure (Figure 1):

First, duplicates were removed, leading to the identification of 655 unique papers. Second, title and abstracts were individually screened, and papers presenting one of the exclusion criteria determined through the PICOS procedure were removed [i.e. articles without eye tracking measure, without addictive substance-related measure, without human sample (i.e. animal study) or without original data]. When the title/abstract screening did not allow a clear-cut decision regarding the inclusion of the paper, it was included in the full-text reading phase. This step led to the exclusion of 565 papers. Third, the 90 remaining papers were screened through full-text reading, leading to the exclusion of 59 papers, which were either primarily focusing on other substance use or psychiatric/neurological disorders (using alcohol-related variables as control measures), or which did not propose any acute alcohol administration or evaluation of alcohol intoxication. This procedure ended up in the inclusion of 31 papers in the systematic review process. For the sake of clarity and despite some overlap across processes in several studies, we have decided to organize the description of the papers in subparts, each focusing on one type of cognitive process. Following the classical categorization used in neuropsychological studies, and notably in literature reviews describing the neuropsychological correlates of alcohol-related disorders (e.g., Carbia et al., 2018; Oscar-Berman et al., 2004; Stavro et al., 2013), we will successively present the studies focusing on perceptive/visuomotor processes (i.e. the ability to perform low-level sensory visual processing, including visual acuity, and to coordinate the motor sequences leading to eye movements), attentional bias (i.e. the preferential processing of alcohol-related stimuli, leading to the hijacking of attentional resources by these stimulations), memory (i.e. the ability to correctly encode, store and retrieve, at short or long term, the internal or external stimulations perceived), and executive functions (i.e. the high-level cognitive functions including inhibition, updating, flexibility and planning, allowing to propose adaptive behaviors and efficient decision making).

Finally, the fifth section will present the studies which were not focused on the exploration of a specific cognitive process but were rather using eye tracking as a tool to clarify the efficiency of interventions aiming at reducing alcohol consumption.

2.2. Methodological quality assessment

The methodological quality of each study was conducted using an adapted version of the "quality assessment tool for observational cohort and cross-sectional studies", developed by the National Heart, Lung and Blood Institute (NHLBI, 2014). This 11-item scale, widely used in various research fields, appears as appropriate for the type of cross-sectional studies considered in the present paper. However, as one item of the original scale was not pertinent here (i.e. item 13: "Was loss to follow-up after baseline 20% or less?"), this item has been removed from the evaluation. Moreover, as several key items related to participants' selection (item 4), statistical analyses (item 5), exposure measures (item 9), outcome measures (item 11) and confounding variables (item 14) included several sub-questions, they have been split in separated items. The final methodological assessment scale used here comprised 20 items with a binary answer (Yes/No), leading to a maximum score of 20. For each study, a percentage score (i.e. number of items with a "Yes" answer divided by 20) was computed, leading to a global quality rating (i.e. poor for scores below 50%, fair for scores between 50 and 69%, good for scores between 70% and 79%, strong for scores of 80% and beyond, adapted from Black et al., 2017). The Supplementary Table 1 reports the score obtained for each study on each item, as well as the global quality ratings.

2.3. Data extraction and synthesis

A systematic data extraction procedure was used to individually determine the main characteristics of each paper, regarding 5 categories of variables (adapted from the PICOS procedure): (1) Population (sample size, age, gender ratio, exclusion criteria); (2) Exposures (psychiatric/neurological diagnosis or (sub-)clinical classification, alcohol-consumption measure, psychopathological comorbidities); (3) Comparator (control group presence and size, matching variables); (4) Experimental design (processes measured, tasks, stimuli, eye tracking indexes); (5) Outcomes (main results, limitations, key conclusions). A comprehensive synthesis of the data extracted from each study is presented in Table 1.

3. Results

3.1. Quality assessment

Among the 31 studies included (Table 1 and Supplementary Table 1), 9 were considered as presenting poor quality, 19 fair quality, and 3 good quality, according to the assessment criteria selected. Most of these studies proposed a quite large sample size, with a good control of acute alcohol consumption level through standardized alcohol intoxication procedures and efficient blood alcohol concentration (BAC) control (directly through blood measures or most often through reliable breathalyzer), and several explorations proposed at least 2 levels of alcohol intoxication to determine the modification of eye movements following mild versus high BAC. The implementation and analyzes of eye tracking measures were globally good, most studies using classical protocols (e.g., visual probe task) and focusing on well-established eye tracking indexes (i.e. number of fixations, saccadic properties, dwell time). The main limits of those studies were related, on the one hand, to the lack of justification of the sample size and of power or effect size

computation to estimate the strength of the statistical results obtained, and on the other hand to the lack of control on chronic alcohol consumption. Indeed, as they were centrally interested in the effects of acute alcohol consumption, those studies usually proposed a very superficial evaluation of chronic alcohol consumption habits, and selected their sample in the general population without considering such criteria. As the few studies which simultaneously considered acute and chronic alcohol consumption showed strong interactions between these 2 factors when considering eye movements, the potentially massive but unmeasured variation in alcohol consumption pattern among the participants included in these studies might have strongly biased the results obtained. Finally, a large proportion of studies did not take into account variables which might have influenced eye tracking measures (e.g., psychopathological comorbidities, medication, and family history of alcohol-related problems).

3.2. Main outcomes

These studies mostly explored the influence of acute alcohol consumption (used as independent variable) on a vast range of abilities, encompassing perception, attentional bias, memory and executive functions. In order to avoid an exhaustive presentation of the alcohol administration procedure performed in each study, the methodological details related to alcohol administration are presented in the Supplementary Table 2. Some studies conversely used acute alcohol consumption or effects as dependent variables, by exploring the influence of alcohol devaluation (in the attentional bias section), responsible drinking messages or drug intake (in the prevention section) on drinking behavior (ad libitum consumption following experimental manipulation), rather than as independent variable (and thus did not administrate alcohol to participants before the experiment).

3.2.1. *Perceptive and visuomotor abilities*

Eight studies have measured the influence of acute alcohol consumption on perceptive or motor processes. Schmääl et al. (2000) initially tested the impact of acute consumption on dynamic visual acuity, related to the ability to maintain efficient visual orientation during movements of the body and/or of the external environment. This study specifically explored how alcohol modifies eye movements and visual acuity (with eyes closed or while seeing a stationary target) during vertical oscillations of the whole body in a within-subject design with 3 time points: before alcohol consumption, just after ethanol intake and 40 minutes later. No significant BAC differences were observed between these 2 last conditions, which were thus merged in the analyses. In the eyes closed condition, acute alcohol consumption increased the amplitude of vertical eye movements during body oscillations. Moreover, in the eyes opened condition, alcohol intake increased phase shift (i.e. the lag between the body movement and the eye movement performed to adapt this body change) and lowered dynamic visual acuity, thus offering the first eye tracking insights on the influence of acute ethanol consumption on the velocity of eye movements. Another key visual function is depth perception, and the influence of acute alcohol consumption on this ability has been tested by Nawrot et al. (2004). The monocular perception of depth is notably accomplished using motion parallax (i.e. the fact that an object appears to move faster when it is closer from the observer), and it has been suggested that this ability might rely on the slow eye movements system. A battery of visual tests evaluating depth perception, smooth pursuit and compensatory eye movements (i.e. slow eye movements produced to maintain the fixation on a target during head translations) was administered to participants, first in a sober test and then after acute alcohol consumption. Alcohol intoxication

centrally reduced the accuracy of slow eye movements requested to perform a smooth pursuit, leading to higher rates of compensatory fast saccades. This impact on the slow eye movement system led to increased motion parallax thresholds, themselves leading to reduced depth perception from monocular indices (while the perception of depth through binocular stereopsis was preserved). While BAC strongly varied across participants, this study thus reinforces the proposal that basic and automatic eye movements are reduced under high alcohol intoxication. This assumption has been further reinforced by Romano et al. (2017) who examined whether alcohol intoxication could provoke gaze-evoked nystagmus, a low-level oculo-motor impairment usually observed in cerebellar dysfunctions, characterized by increased centripetal eye drift (corrected through centrifugal saccades). They measured gaze-holding (i.e. the ability to fixate a flashing red light moving in the horizontal axis at various peripheral eccentricities, up to 40°) in a 2-condition (sober versus intoxicated) within-subject design. Alcohol intoxication led to gaze instability: higher eye drift velocity was observed in this condition, characterized by faster centripetal drifts increasing with increased eccentricities. Alcohol intoxication thus appears to be associated with reduced cerebellar functioning, notably impacting basic visual abilities. A last study examining the modification of automatic ocular functions by alcohol intoxication (Ma et al., 2011) focused on the modification of the pupillary diameter before and after acute alcohol consumption. Results showed a significant increase of pupillary diameter one hour after high acute alcohol intake, followed by a reduction of this diameter 24 hours after. In view of the very low methodological quality of this study (unclear experimental objectives, limited sample size, absence of detailed methodology, absence of BAC measure), these results have to be considered as very preliminary.

Proposing a well-controlled alcohol-consumption procedure (within-subject design with 3 sessions, each related to a specific BAC level), King & Byars (2004) explored for the first time higher-level eye movements and showed that smooth pursuit, as well as saccadic latency and velocity (during a prosaccade task) are impaired only for high alcohol intoxication levels. Importantly, this effect did not strongly vary according to chronic alcohol consumption, as both light social and heavy drinkers were significantly impaired during the descending (i.e. post-peak) BAC phase (105 minutes after alcohol consumption). The only difference between light social and heavy drinkers was indeed that, in the smooth pursuit task, the former were mostly impaired during the late part of the ascending (i.e. pre-peak) BAC phase (45 minutes after alcohol consumption, just before BAC peak) while the latter were mostly impaired during the initial ascending BAC phase (15 minutes after alcohol consumption). Similar results regarding the influence of low alcohol intakes were obtained more recently (Schmitt et al., 2013) using a repeated measure (15, 30, 45 and 60 minutes after alcohol administration) of eye movements in a prosaccade paradigm (where participants have to produce fast saccades towards a peripheral target appearing on one side of the screen) among 40 healthy individuals. Alcohol intoxication (which strongly varied across participants) was associated with lower saccadic accuracy (particularly at the end of the ascending BAC phase, just before reaching the BAC peak) and reduced saccadic velocity compared to pre-intoxication performances. However, eye movement's impairment of intoxicated individuals did not reach significance when compared with an age-matched sober group, raising doubts about the validity of such measures to differentiate sober and intoxicated individuals. Here again, the high inter-individual variability in the BAC levels obtained, as well as the unreliability of the comparison with the control group, hamper to draw strong conclusions. Two studies (Roche & King, 2010; Roche et al., 2014) deepened the exploration of the joint influence of acute and chronic alcohol consumption

on eye movements initiated by King & Byars (2004). Roche & King (2010) used a similar design (within-subject protocol with 3 sessions inducing various alcohol intoxication levels) to compare eye movements performance in light and heavy drinkers. They first observed a global impairment in ocular abilities (smooth pursuit gain, prosaccadic latency, velocity and accuracy) at peak BAC, this deficit still being observed 3 hours after alcohol consumption for the high intoxication condition. Moreover, they showed that chronic alcohol consumption pattern did not influence the deficit related to smooth pursuit or antisaccade tasks (i.e. inhibition tasks in which participants have to perform saccades in the opposite direction of a target appearing on one side of the screen). Conversely, light drinkers presented stronger deficit in prosaccadic latency, accuracy and velocity than heavy drinkers. Moreover, participants with a positive history of alcohol dependence among close family members presented better performance in smooth pursuit gain during alcohol intoxication. It thus seems that the tolerance induced by heavy drinking, as well as the presence of family alcohol-related disorders, might partly reduce the ocular impairments generated by alcohol intoxication. Roche et al. (2014) aimed at replicating those results using a similar design (but only comparing sobriety and high intoxication) in a second independent cohort of heavy drinkers. The intra-group results (i.e. within-subject comparison between placebo and alcohol conditions) observed in the initial study were mostly replicated by identifying, particularly at peak BAC (one hour after alcohol consumption), impaired smooth pursuit gain, prosaccade latency/velocity, and antisaccade latency in heavy drinkers. Conversely, and in contradiction with previous results, an absence of deficit was found for prosaccade accuracy and antisaccade velocity, while a marginal impairment was found for antisaccade accuracy. The direct comparison between cohorts did not identify any significant difference, suggesting a coherent and reproducible pattern of eye movements' deficits under alcohol intoxication in heavy drinkers.

3.2.2. *Attentional bias*

Eight studies used eye tracking measures to explore attentional biases following alcohol intoxication. Field et al. (2005) offered the first exploration of this topic, in an indirect way as they measured the impact of acute alcohol consumption on smoking-related bias in regular smokers through a classical visual probe task with smoking-related cues. This task is based on the simultaneous presentation of an image containing a smoking-related cue (on one side of the screen) and a matched image without such cue (on the other side of the screen), followed by the presentation of a target (an arrow pointing upside or downside) to be processed (the participant had to detect the orientation of the arrow as fast and accurately as possible), alternatively appearing at the same position than the smoking-related or non-smoking related image. At the behavioral level, a smoking-related attentional bias is evidenced if the participant is faster to process the target when it appears at the same position than the smoking-related image, as it suggests that more attentional resources were attributed to this image (i.e. that a preferential processing was applied to smoking cues). Eye tracking indexes are considered as useful to determine the processes underlying such preferential processing (e.g., more frequent initial fixation on the smoking-related cue, higher number of fixations, and/or higher dwell time). The authors showed that a low dose of alcohol did not impact the initial fixation but increased dwell time on smoking cue (i.e. the maintenance of attention on these cues), in relation with higher smoking craving and self-reported smoking pleasantness. These results suggest that alcohol intoxication reinforces the incentive value of smoking-related cues, leading to a stronger attribution of attentional resources towards these cues (which is further indexed at the behavioral level, as smoking-related attentional bias only appeared after alcohol consumption). In the same vein,

Marks et al. (2015) explored the increase of attentional bias towards cocaine following various acute alcohol intakes. However, they found that alcohol intoxication did not modify bias intensity, as the attentional bias indexed by increased dwell time towards cocaine cues was robust but stable across all experimental conditions. As cocaine craving increased after alcohol intake, it appears that attentional bias and craving are not strongly related in this population, and might not rely on similar processes: alcohol might increase the incentive value of cocaine (indexed by higher craving) without modifying its salience (indexed by unmodified attentional bias). Interestingly however, this bias was undetectable at the behavioral level (i.e. no faster reaction times for targets appearing on the same side than cocaine-related cues), which underlines the usefulness of eye tracking measures to detect attentional biases in addictive behaviors.

The first direct exploration of alcohol-related attentional bias during alcohol intoxication has been proposed by Schoenmakers et al. (2008), who used a similar design (visual probe task during sobriety or low alcohol intoxication) among heavy drinkers, but with alcohol-related stimuli (alcohol-related scenes, paired with non-alcohol-related scenes) instead of smoking-related stimuli. No difference between alcohol-related and control images was observed for initial fixation and dwell time in the placebo (non-alcoholic) condition, showing an absence of attentional bias among heavy drinkers during sobriety. Conversely, acute alcohol consumption induced a significant attentional bias towards alcohol-related pictures at behavioral and eye tracking levels: these pictures were both more frequently targeted by the initial fixation and associated with longer dwell time than control pictures. A significant positive correlation was also observed between behavioral (faster reaction times for the targets appearing on the same side than the alcohol-related picture) and eye tracking (proportion of dwell time focused on the alcohol-related picture) correlates of attentional bias during

alcohol intoxication, showing a good coherence between these indexes. The intensification of attentional bias towards alcohol during alcohol intoxication was not confirmed in a more recent study (Miller & Fillmore, 2011) also using a visual probe task among heavy drinkers, but differentiating 3 alcohol intake levels. While behavioral results did not index any attentional bias whatever the experimental condition, higher dwell time for alcohol-related cues was already present in the placebo condition, and it remained constant at the 2 levels of alcohol intoxication. Results also showed a linear decrease of the accuracy and velocity of the saccades towards targets according to the intensity of alcohol intoxication, thus confirming the impact of such intoxication on the perceptive abilities related to eye movements, as described in the previous section. Fernie et al. (2012) proposed a similar design but with a direct comparison between light and heavy drinkers. They showed that heavy drinkers are characterized by a strong attentional bias (indexed by longer dwell time for alcohol-related pictures, but not present at the behavioral level), independent of acute alcohol consumption, which is interpreted as indexing a tolerance effect towards alcohol consumption in this population. Conversely, light drinkers only presented this attentional bias when under the influence of alcohol. Moreover, the increase of attentional bias following alcohol consumption did not modulate alcohol seeking behavior (in a subsequent task where participants were invited to drink in a bogus taste test), thus questioning the influence of attentional bias on actual alcohol consumption in ecological contexts. A last study directly focusing on the variation of the attentional bias according to acute and chronic alcohol consumption (Weafer & Fillmore, 2013) used the same visual probe task in a within-subject design among light and heavy drinkers, but with 2 acute alcohol levels. They confirmed that heavy drinking is associated with a significant attentional bias (higher dwell time for alcohol-related images) during sobriety, this bias being proportional to the intensity of chronic alcohol consumption. They also showed that the bias gradually

decreases when BAC levels increase in this population (while it remained moderate and stable in light drinkers), the authors explaining this result by the fact that attentional bias would mostly be intense during the craving period preceding an alcohol consumption episode. Attentional bias would thus be an important factor predicting the start of a drinking episode rather than its perpetuation once initiated, but this conclusion is at odds with the results obtained in other studies (Fernie et al., 2012; Miller & Fillmore, 2011, and mostly Schoenmakers et al., 2008). More broadly, in view of the very diverse and often contradictory results obtained across the 4 last studies mentioned, it appears that the joint influence of acute and chronic alcohol consumption patterns on the attentional bias remains to be clearly defined, as several uncontrolled biasing factors might have influenced the available results. Finally, 2 studies explored how an alcohol devaluation procedure (rather than acute alcohol consumption *per se*) can modify the attentional bias towards alcohol-related stimuli, and how this modification can itself impact actual alcohol-seeking behaviors (as it has been hypothesized that attentional bias could play a causal role in the development of excessive alcohol consumption). Rose et al. (2013) used the concurrent choice task (Hogarth & Chase, 2011) in which participants are confronted with pairs of stimuli (alcohol beverage on one side of the screen, soft drink on the other side) and have to decide, for each pair, their preferred stimulus, while eye movements are recorded. This task was performed before and after a devaluation procedure in which participants drank an unmodified (no devaluation control condition) or adulterated (devaluation condition, where a bitter-tasting liquid is added) alcoholic drink (in a between-subject design). The devaluation condition was associated with a reduction of the desire to drink alcohol, confirming the efficiency of this procedure. Centrally, concurrent choice task results showed a reduction of the preference for alcohol after devaluation. This was combined with a decrease of the attentional bias towards alcohol, indexed by reduced percentages of

initial fixation, dwell time and last fixation on alcohol-related pictures (which was not observed in the non-devaluation condition). It thus appears that alcohol devaluation simultaneously reduces behavioral preference for alcohol and attentional bias, but complementary analyses showed that the reduction of attentional bias only partially mediates the effect of devaluation procedure on alcohol preference, putting into question the causal relationship between attentional bias and actual alcohol-related behaviors. A similar study (Rose et al., 2018) recently deepened the exploration of the links between attentional bias and alcohol-related behaviors by recording eye movements during the Pavlovian-to-instrumental transfer phase (i.e. the process by which a reward-related cue stimulates reward-seeking behavior, even though the cue and response have not previously co-occurred) of the concurrent choice task. In this version of the task, participants first had to choose between alcohol and soft response keys (acquisition phase) to collect points for each substance (as they were told that these points will be converted into real drinks at the end of the experiment). Then, they still had to choose but they did not collect points anymore (extinction phase). This phase was followed by the Pavlovian-to-instrumental transfer phase, where they had to choose without collecting points, but with a simultaneous presentation of alcohol and/or soft drinks pictures. A final phase (reacquisition phase) was based on the reintroduction of the outcomes (collection of alcohol/soft points). This task was preceded by a devaluation/no-devaluation manipulation similar to the one described above (Rose et al., 2013), and was followed by a bogus taste test to measure *ad libitum* drinking behaviors. This procedure allowed to show that alcohol devaluation reduced all goal-directed alcohol choices, namely alcohol craving, *ad libitum* alcohol consumption, as well as alcohol preference in all phases of the concurrent choice task. However, a cue-elicited priming effect persisted in the Pavlovian-to-instrumental transfer phase: alcohol choices were reduced after devaluation, but remained more frequent when pictures of alcohol

drinks were presented. This differential effect suggests a dissociation between goal-directed and cue-elicited choices. Eye tracking measures showed, in perfect line with the previous study, that alcohol devaluation led to reduced attentional bias towards alcohol stimulations, indexed by lower initial fixations and dwell time for alcohol than soft cues. Moreover, these attentional bias changes fully mediated the influence of alcohol devaluation on cue-elicited alcohol choice, but also on *ad libitum* alcohol consumption and alcohol preference. It is finally worth noting that, in the no-devaluation condition, no attentional bias was observed (i.e. no initial fixation or dwell time differences between alcohol and soft cues).

3.2.3. Memory

Memory abilities during alcohol exposure were explored in 5 studies using eye tracking. Harvey et al. (2013a) measured the changes occurring to the visual exploration and memorization of complex scenes after alcohol intoxication, in a between-subject 2-session design. Participants were first administered a soft or alcoholic drink and were then asked to freely explore 5 photographs of the same male individual committing legal offenses, while their eye movements were recorded. The second session was performed the day after, during which participants had to perform an identification task (i.e. recognizing the individual presented the day before from series of faces) as well as a test of general recognition memory (binary judgments on the contents of the images presented the day before). No group difference was observed for identification or recognition tasks (although individuals in the alcohol condition were less confident in their answers), suggesting that alcohol consumption did not strongly interfere with memory encoding. Regarding eye tracking measures, alcohol intoxication did not modify the number of fixations and dwell time related to the central or peripheral parts

of the pictures. In conclusion, and despite a large variance in the actual BAC presented by participants that hampers to clearly state the precise influence of alcohol, alcohol intoxication does not seem to modify the visual exploration and memory encoding of complex scenes. This goes against the alcohol myopia theory (Steele & Josephs, 1990) stating that alcohol intoxication would reduce attentional resources, leading individuals to focus on central or salient cues and neglect peripheral ones. Another study from the same group (Harvey et al., 2013b) surprisingly led to the opposite conclusion. They used a similar 2X2 between-subject design to test the influence of alcohol intoxication (versus placebo) on the encoding and memory of matched salient (i.e. police assault during a protest) or non-salient (i.e. public musical concert) pictures. Alcohol intoxication did not have any impact on the number, amplitude or velocity of saccades, but the number of fixations and dwell time were higher among participants confronted with the emotionally salient scene. More centrally, alcohol intoxication increased this effect by further augmenting the visual focus (number of fixations and dwell time, but not mean single fixation duration) on the central components of the scene (compared with the placebo group) in both salient and non-salient conditions. The behavioral counterpart of this eye movement effect was that acute alcohol intoxication reduced the number of recalled items in the memory test performed the day after. While this memory deficit was independent from the peripheral or central position of the recalled items, this led the authors to propose that their results support the alcohol myopia theory. They also suggested that such contradictory results in comparison with their previous study (Harvey et al., 2013a) might be driven by differences in the stimuli chosen or memory evaluation, but do not offer convincing arguments to support this assumption as the procedures used in these 2 studies were actually very close. A last study performed by the same author (Harvey, 2014) explored in a within-subject design how acute alcohol consumption modifies visual scanning and encoding of facial stimuli during a

memory task. The 2 sessions (alcohol intoxication versus placebo), performed on successive days, were identical: participants first took part in an encoding phase during which eye movements were recorded while they were confronted with 20 faces from their (Caucasian) or another (Indian) ethnical group, after drinking an alcoholic or soft beverage. The recognition phase occurred 6 hours later, based on binary identification judgments (i.e. seen in the encoding phase or not) of 40 faces. Beyond the replication of largely established data demonstrating that sober participants mostly focus on eye (and to a lesser extent on nose) regions during face encoding, this study showed that alcohol intoxication modified this exploration: dwell time for the nose region was increased among intoxicated individuals, with conversely a reduced dwell time for the eye region in this condition. Moreover, once intoxicated, participants presented reduced visual exploration (i.e. saccadic distance) and lower number of fixations (without difference in dwell time). Yet, this narrowing of visual scanning did not impact memory performance, again questioning the influence of visual exploration on encoding efficiency.

Two studies addressed the influence of alcohol intoxication on memory through a different perspective, by investigating advertisements' visual exploration and encoding in alcohol-related contexts. Orquin et al. (2014) performed 2 experiments exploring the modulation of attention and advertisement encoding by acute alcohol intoxication. In the first experiment, they manipulated the perceptual (pictorial elements) and conceptual (text) load of advertisements and measured the visual scanning pattern for various elements of the advertisement (headline, logo, image, text). An ecological procedure was used regarding alcohol intoxication, as the authors did not administer alcohol but rather recruited participants in drinking contexts. Very various BAC levels were measured, leading to a low control on the specific influence of alcohol intoxication on the results. The main impact of alcohol intoxication was an

increase of the attentional focus on perceptual elements (centrally for brand logo), independently of the perceptive/conceptual load ratio. This attentional bias towards the logo was associated with reduced processing of the conceptual parts (headline or text) of the advertisement (longer first fixation latencies and reduced dwell time). The second experiment used the exact same methodology but with a procedure closer to real life (by presenting advertisements in a magazine rather than as isolated pictures). It showed that alcohol intoxication reduced the attentional capture of advertisement's parts (particularly for the logo, which is in contradiction with the first experiment), leading to a reduced brand name recall (proportional to the intensity of alcohol intake) in the following memory task. Conversely, alcohol intoxication increased the number of fixations on the advertisement's text, which was interpreted as reflecting the fact that intoxicated individuals have reduced reading abilities and thus needed more time to read the text. To sum up, those 2 experiments suggested that alcohol intoxication can increase the attention towards perceptual elements in a forced advertisement exposure, while it actually reduces this attentional focus during voluntary exposure. Ellert et al. (2014) ended up with opposite conclusion in a study focused on the visual exploration and encoding of advertisements presented during sport programs on television. Alcohol intoxication was achieved by asking half of the participants to drink one liter of beer at their own rhythm (the others remaining sober), without any measure of the actual BAC level when performing the task. All participants then watched a 5 minute video of a football match containing advertisements, during which eye tracking measures were conducted, and then performed a recall task concerning the content of the video. It was shown that intoxicated participants presented lower number of fixations but higher dwell time on advertising, combined with a better brand recall. In view of the very weak methodological quality of this study

regarding acute and chronic alcohol consumption measures, it appears impossible to draw valid conclusions from the presented results.

3.2.4. Executive functions

The links between alcohol intoxication and ocular abilities have been explored in 4 studies focusing on the inhibitory control of eye movements, as well as in 3 studies exploring higher-order executive functions involved in efficient car driving. Regarding the first series of studies, an initial exploration (Vorstius et al., 2012) used a within-subject design to explore the influence of alcohol intoxication on a double-step task, based on the presentation of a stimulus followed in 75% of the trials by another stimulus after a short time interval (40, 70 or 100ms), and thus requesting saccadic reprogramming (i.e. cancelling the saccade towards the first stimulus to perform a saccade towards the second one). Alcohol intoxication increased first saccade latency and velocity, as well as the time needed to reprogram eye movements (i.e. to cancel the first saccade and prepare an adjusted one targeting the second stimulus), leading to increased rates of 2-step responses (namely the presence of 2 saccades due to the inability to cancel the first one when a second stimulus appears). The authors interpreted this deficit as reflecting impaired automatic oculomotor processing, but it appears that alcohol intoxication centrally impaired the ability to reprogram eye movement sequences, this reprogramming at least partly requesting controlled processes (i.e. inhibition to stop the first saccade, flexibility to program a second modified saccade). A neuroimaging study (Marinkovic et al., 2013) more directly focused on alcohol intoxication's impact on inhibitory control of eye movements in a within-subject prosaccade/antisaccade paradigm. They identified the frontoparietal brain network involved in

saccadic conflict processing but also showed that mild alcohol intoxication strongly disrupted saccadic conflict management: while no difference was observed at the behavioral level, increased saccade latency was measured following alcohol intoxication when an antisaccade was required (without any difference regarding prosaccades). This impairment was underpinned by reduced activity in the dorsal anterior cingulate cortex, a key region for cognitive control (Heilbronner & Hayden, 2016). Roberts et al. (2014) also explored, in a within-subject design, the modulation of eye movement's inhibitory control by alcohol intoxication in a delayed ocular response task among heavy drinkers. In each trial of this task, participants had to fixate a central point, then a peripheral distractor stimulus briefly appeared and participants were told to withhold performing a saccade towards this stimulus, this saccade being requested only after the disappearance of the fixation point (800-1200ms after distractor's disappearance). This task assessed inhibitory control of attention by testing the ability to delay a reflexive saccade towards a stimulus, and premature saccades (i.e. saccades towards the location of the distractor stimulus before the disappearance of the fixation point) indexed failed inhibition. Alcohol intoxication significantly increased the number of premature saccades, but also augmented saccadic latency and reduced saccadic accuracy of correct saccades (i.e. those appearing after the disappearance of the fixation point). This study also included the classical visual probe task (only at behavioral level), which allowed to demonstrate the presence of an attentional bias towards alcohol-related stimuli, and centrally to show that a positive correlation between chronic alcohol consumption and inhibitory control's impairment during alcohol intoxication was only observed among participants presenting a strong attentional bias. In other words, it appears that a joint increased attentional bias and decreased inhibitory control during alcohol-related processes are associated with stronger chronic alcohol consumption. Another approach of the executive control on eye movements during alcohol intoxication has

been proposed using the Visual Maze Task (Silva et al., 2017), in which participants had to escape from a maze by making efficient choices regarding the path to be followed at each intersection. This task (Santos et al., 2014) is supposed to measure how participants use visual and executive abilities to choose the right exit, but the very diverse ocular (visual scanning strategy, saccades and dwell time towards the various maze elements) and executive (inhibition, flexibility, decision making) abilities requested to perform the task make it difficult to identify the key parameters at play. Results obtained in a within-subject design among heavy drinkers showed that acute alcohol intoxication was associated with longer first fixation latency, globally higher number of saccades and fixations and higher mean/total dwell time during the Maze task, together with a specific increase of the number of fixations and dwell time on key regions (i.e. intersections where a choice had to be made). As these eye movements parameters were only related to a global increase in the time needed to perform the task, it is impossible to state whether the modification of the visual scanning pattern during alcohol intoxication indexed an impairment of specific executive functions leading to reduced performance, or was merely reflecting globally reduced/slower ocular processing or strategical changes.

Regarding the second series of studies, Massimore & Spilich (2001) explored in a between-subject design how alcohol intoxication modified the visual exploration of pictures presenting driving scenes from the driver's perspective. They showed that mild alcohol intoxication reduces the efficiency of visual exploration, and centrally lowers the number of fixations (without modifying dwell time) on the most important parts of the scene for safe driving (e.g., pedestrian crossing the street). Despite a very low sample size and methodological flaws, this study thus suggested that alcohol intoxication might lower the efficiency of visual processing while driving, potentially increasing the time needed to react to the emergence of dangerous situations. Lamers & Ramaekers (2001) also

measured the influence of alcohol (combined or not with marijuana smoking in a within-subject design) on eye movements during real car driving (i.e. 15 km drive in various urban roads). Driving performance was rated by a professional evaluator, and eye tracking was used to measure visual scanning (operationalized as the number of time the participant checked for traffic at each road intersection). Data showed an absence of influence of mild alcohol intoxication (alone or combined with marijuana smoking) on driving performance and visual scanning at road intersections, with the exception of a slightly reduced visual search frequency in the combined alcohol/marijuana condition. This absence of significant effect might however at least partly be the consequence of a very limited use of eye tracking measures, as no classical index (e.g., dwell time, saccadic velocity, number of fixations on pertinent information) were reported. A more recent study (Marple-Horvat et al., 2008) addressed a related issue by determining the impact of acute alcohol consumption on the visuo-motor coordination involved in car driving. In many everyday life situations, eye movements are used to guide motor actions, and this is particularly true for car driving, where eye scanning allows to adjust steering wheel control. A within-subject design tested the modification of the eye/hand movements coordination by alcohol intoxication, and its impact on fitness to drive in a driving simulator. Despite a limited statistical power due to small sample size and large performance variations across participants, data showed that eye movements clearly guided steering (i.e. eye movement to the left before turning the wheel to the left), and that this coordination was progressively deteriorated with the increase of BAC level: due to shorter eye movements, the degree of linkage between eye and steering movements was reduced even at mild BAC, and further declined in a sharper way for higher BAC. The behavioral correlate of this reduced coordination was a progressively increased probability of car crash during driving simulation (following BAC intensification).

3.2.5. Prevention

Two studies used the tendency to spontaneously consume sham alcoholic beverages (i.e. alcohol-free beer or wine) as a dependent variable, by measuring how environmental factors and exposure to responsible drinking messages can modify drinking behaviors in non-problem drinkers. In a series of 4 experiments, Moss et al. (2015) explored how alcohol prevention posters and brief online exposition to responsible drinking messages modulated ecological sham alcohol consumption (free drinks choice in a simulated bar environment). They mostly showed that consumption actually increased after being exposed to prevention posters (this negative impact being partly reduced by the simultaneous presentation of online responsible messages), leading to the conclusion that materials promoting responsible drinking might be counter-productive by increasing real life alcohol consumption. Eye tracking measures complemented these results by showing that participants globally dedicated low visual attention (i.e. low rates of initial fixation and low dwell time) to prevention messages (instead focusing on the positive pictures also present in the posters), which might explain the increased intakes observed afterwards. Frings et al. (2018) recently used a similar methodology to explore how environmental context (i.e. bar laboratory versus classical laboratory) influences the impact of prevention posters on drinking behaviors. It appeared that an environment containing a large range of alcohol-related stimuli, namely the bar laboratory, was associated with reduced number of fixations and lower dwell time on prevention posters (compared to control health-related ones), which was not found in the classical laboratory (where alcohol-related cues were rare). This study thus suggested that prevention campaigns should take place in contexts where alcohol-related stimulations are sparse rather than in drinking contexts (where

individuals do not pay attention to responsible drinking posters). It should be noted that the increase of consumption following the confrontation with alcohol prevention poster found in the previous study (Moss et al., 2015) was not replicated here. A last study (Childs et al., 2012) explored how varenicline (a partial acetylcholine receptor agonist used in tobacco cessation therapy) could reduce alcohol consumption by increasing the aversive effects related to acute alcohol intakes. A within-subject design tested the modification of subjective (e.g., feeling high, craving, nausea) and objective (e.g., heart rate, eye movements) responses to alcohol intoxication by varenicline administration in 15 healthy social drinkers, leading to 6 experimental conditions [3 alcohol levels X 2 drug types (0.2 mg of varenicline or placebo)]. Smooth pursuit (i.e. following a target moving horizontally on the screen in a predictable sinusoidal way for 75 seconds), prosaccade and antisaccade tasks were used to evaluate the gain, latency, velocity and accuracy of eye movements at 3 time points: before administering varenicline/placebo, 120-150 minutes after, and 45-60 minutes after alcohol administration (which occurred 180 minutes after drug intake). Eye tracking-related results showed that high alcohol intoxication impaired gain in smooth pursuit and increased pro- and antisaccades latencies. However, these deficits were partly compensated by varenicline, which increased the subjective aversive effects of alcohol but simultaneously reduced alcohol-related eye movements' impairments (saccadic slowing down and lower accuracy). Imprecisions in the methodological description of the timing of drug/alcohol intakes as well as very limited sample size nevertheless call for caution when interpreting these results.

4. Synthesis of the results

- *Perceptive and oculomotor abilities*: Alcohol intoxication decreases the oculomotor response related to changes in body position (Schmäl et al., 2000), impairs depth perception from motion parallax (Nawrot et al., 2004), increases pupillary diameter (Ma et al., 2011) and might impair smooth pursuit as well as saccadic latency/velocity [King & Byars, 2004, but contradictory results have been reported (Schmitt et al., 2013)]. Chronic heavy drinking, conducting to increased alcohol tolerance, might lead to a partial reduction of these eye movement impairments (Roche & King, 2010), but heavy drinkers nevertheless present a reproducible pattern of eye movement impairments during high alcohol intoxication (Roche et al., 2014). Varenicline appears to reduce the eye movements deficits induced by high intoxication (Childs et al., 2012). While all perceptive and oculomotor abilities have not yet been explored through eye tracking measures, the currently available results suggest that alcohol intoxication leads to a global impairment of these abilities, centrally through its strong impact on cerebellar functions (Romano et al., 2017). Indeed, on the one hand, it is well established that most neural commands leading to eye movements are generated by a brain network in which the cerebellum occupies a key position (Nakamagoe et al., 2000). Cerebellar structures are notably responsible for the coordination and precision of the visuo-motor abilities needed to perform efficient saccades and smooth pursuit (Quinet & Goffart, 2015). On the other hand, the influence of alcohol intoxication on cerebellar functioning is also well known: alcohol leads to a global inhibitory effect on the cerebellum (through the perturbation of the excitatory/inhibitory balance) related to an increased activity of the inhibitory GABA neurons (Santhakumar et al., 2007) and thus to hypo-activation and reduced blood flow (Volkow et al., 1988). The cerebellum actually appears as one of the brain regions being the most sensitive to alcohol effects (Bühler & Mann, 2011), notably because

acute alcohol intoxication alters the functioning of Purkinje cells densely populating this structure and responsible for motor coordination and gaze-related processes (Carta et al., 2006; Servais et al., 2005). As a whole, and while eye movements are obviously generated by a neural network encompassing several subcortical and cortical areas, the cerebellum appears as the hub structure to explain the visuo-motor impairments following alcohol intoxication.

- *Attentional bias*: Alcohol intoxication has been repeatedly associated with an attentional bias towards alcohol-related cues, but results are not coherent regarding the influence of chronic consumption on this bias following acute consumption: it has first been suggested (Schoenmakers et al., 2008) that the bias would be absent during sobriety, even in heavy drinkers, while more recent works have argued that alcohol intoxication does not influence the attentional bias in heavy drinkers (Miller & Fillmore, 2011) or even reduces it (Weafer & Fillmore, 2013). Conversely, alcohol intoxication increased the attentional bias in light drinkers (Fernie et al., 2012). An alcohol devaluation procedure reduces this alcohol-related attentional bias (Rose et al., 2013; 2018). Moreover, alcohol intoxication also modulates the preferential processing of other substances by reinforcing the attentional bias towards smoking-related cues in smokers (Field et al., 2005) and increasing cocaine craving (without influencing cocaine-related attentional bias) in cocaine users (Marks et al., 2015). As a whole, while the presence of an alcohol-related attentional bias has been largely established in several clinical and subclinical patterns of chronic alcohol (Fadardi et al., 2016; Field & Cox, 2008) and constitutes a key component of the current models of addictive disorders (Field et al., 2010; Wiers et al., 2015), and while eye tracking studies confirm that this bias is also present during alcohol intoxication, the modulating effects of the interactions between acute and chronic consumption patterns on this bias remain to be understood.

- *Memory*: Alcohol intoxication might reduce memory encoding through changes in the visual exploration of complex scenes [by increasing the attentional focus on central features (Harvey et al., 2013b)] and faces [by increasing the nose/eyes focus ratio (Harvey, 2014)], but contradictory results have been reported by the same research group (Harvey et al., 2013a). It might also modify the memory encoding of advertisements by reducing the number of fixations but increasing dwell time (Ellert et al., 2014), and by modulating the attentional focus on perceptual features [increasing it during forced exposure but decreasing it during voluntary exposure (Orquin et al. (2014)]. These eye tracking results showing a negative impact of alcohol intoxication on memory are in line with the vast literature describing large scale impacts of acute and chronic alcohol consumption on a wide range of memory systems including working memory, as well as visual/verbal memory encoding and retrieval (see for example Oscar-Berman et al., 2004 or Stavro et al., 2013 for reviews).

- *Executive functions*: Alcohol intoxication impairs saccadic reprogramming abilities (Vorstius et al., 2012) and inhibitory control of saccades (Roberts et al., 2014) in moderate drinkers, and increases fixations as well as dwell time during decision-making tasks (Silva et al., 2017). This reduced inhibitory control is related to lower anterior cingulate activation during saccadic conflict (Marinkovic et al., 2013). In a driving context with high-level executive demands, alcohol intoxication might reduce the eye-motor coordination (Marple-Horvat et al., 2008) and the number of fixations on the important features of a driving scene (Massimore & Spilich, 2001), but other results have shown no influence of acute consumption on visual scanning while driving (Lamers & Ramaekers, 2001). While this exploration of executive functioning is very lacunar, the main deleterious influence of alcohol intoxication on executive functions thus appears to be a reduction of inhibitory abilities, which is coherent with the proposal that inhibition deficits are a hallmark of

alcohol-related disorders. These results observed during acute intoxication are also coherent with those obtained using eye tracking measures in heavy drinkers, as it has notably been shown (Wilcockson & Pothos, 2015) that heavy drinking reduces inhibitory control on saccadic movements, particularly when alcohol-related stimuli are used.

- *Prevention*: In light drinkers, a very limited visual attention is dedicated to prevention messages in posters promoting responsible drinking (Moss et al., 2015), this attention being even lower in alcohol-cue rich environments (Frings et al., 2018). The main conclusion that can be drawn from these studies is thus that alcohol intoxication further lowers the attention towards prevention messages, which has already been shown to be very low among heavy drinkers (e.g., Monk et al., 2015; Yzer et al., 2017). These results strongly question the usefulness of such messages and might lead to a reconsideration of prevention campaigns targeting excessive alcohol consumption.

5. Limits of the current literature

5.1. Alcohol-related measures

Studies exploring eye tracking correlates of acute alcohol consumption were characterized by a massive heterogeneity in the procedure used to compute the administered alcohol dose, but also in the evaluation of the actual BAC level (see Supplementary Table 2). Most of them determined the alcohol dose to be administered on the basis of participants' weight and did not jointly take into account the variations related to age, gender or height, which are crucial factors influencing alcohol diffusion and elimination (Posey & Mozayani, 2007). This limited control ended up in strong inter-individual variations in the BAC levels measured (e.g.,

Harvey et al., 2013a; Nawrot et al., 2004; Schmitt et al., 2013). Several studies did not even measure the BAC level obtained following alcohol administration (e.g., Ellert et al., 2014; Rose et al., 2013; 2018) and the evolution of the BAC level during the task was most often not controlled for. As a whole, the large inter- and intra-study variability in the BAC levels obtained is a crucial limit to compare the available data on alcohol intoxication. Moreover, while some studies simultaneously measured chronic and acute alcohol consumption, most of them did not take into account the influence of chronic consumption on the eye movements observed during alcohol intoxication. Indeed, chronic drinking habits have most often been overlooked and not considered as selection criteria or experimental measures. The few studies that investigated the respective influence of acute and chronic alcohol consumption on the modification of eye movements, while clearly underlining the presence of strong interactions between these 2 factors, showed contradictory results that remain to be clarified (King & Byars, 2004; Miller & Fillmore, 2011; Roche & King, 2010; Schoenmakers et al., 2008).

5.2. Eye tracking indexes

Most studies proposed a direct link between eye tracking indexes and underlying cognitive processes, leading to potential over-interpretations. Indeed, despite the established usefulness of the eye tracking technique, the interpretative gap between the actual indexes measured and the cognitive processes estimated should always be kept in mind. Eye tracking actually allows to measure gaze location, as well as characteristics of the eye movements (e.g., fixation, saccade, pursuit, blink) or of the eye itself (e.g., pupillary diameter), but these measures are not purely reflecting cognitive abilities. Indeed, eye movements' patterns should be

cautiously interpreted as they can be influenced by various bottom-up (e.g., stimuli brightness, color, movement) or top-down (e.g., previous experience, expectations, goals) sources. For example, the widely used prosaccade/antisaccade paradigm is based on the core assumption that the prosaccade part measures saccadic velocity and duration (and is thus mostly related to perceptive/oculomotor abilities and cerebellar functioning), while the antisaccade part is indexing executive functions by measuring the ability to inhibit and/or reprogram saccades (and is thus mostly related to anterior cingulate cortex and frontal areas). However, the potential deficit measured in the antisaccade task can be at least partly influenced by the lower level impairment measured by the prosaccade task (e.g., global modifications of saccadic speed) and, conversely, prosaccade performance can be modulated by higher-level cognitive processes (e.g., erroneous anticipation related to reduced inhibitory control). As a whole, there is an urgent need to clearly disentangle, in each paradigm used, the often multiple cognitive processes involved in order to offer a balanced interpretation of the results observed. Moreover, eye tracking only captures the foveal vision, yet visual stimuli can be processed by the peripheral retina and this processing is even likely to influence the subsequent analysis in foveal vision, in particular when peripheral stimuli have a high salience or are affectively-laden (D'Hondt et al., 2013). Overall, it is therefore very important to carefully choose the task that will be submitted to the participant, as well as the eye tracking measures that will be considered, in order to draw accurate conclusions on the basis of gaze behavior, especially to infer the cognitive processes responsible for the eye movements. For instance, many studies used the dwell time as a measure of interest, considering that the time spent by participants looking at specific parts of the visual scene unambiguously indexed their interest or bias towards these parts. However, longer dwell time or longer fixations can also reflect other factors, and notably cognitive processing difficulty. Actually, fixation durations are on average

200-260ms for reading (Rayner & Pollatsek, 1989) and slightly longer for scene viewing (Holmqvist et al., 2011). Consequently, longer viewing time can reflect more effort to extract the meaningful information (Rayner et al., 1978), as well as drowsiness or low arousal, as postulated by research on vigilance (Chapman & Underwood, 1998). As a whole, most studies using eye tracking measures in alcohol-related disorders have implicitly taken for granted that each eye tracking index is a quite direct reflect of specific cognitive processes, neglecting the current controversies regarding the use of eye tracking measures to assess the targeted cognitive abilities.

6. Perspectives

6.1. Improving alcohol consumption evaluation

The main priority for increasing the methodological quality of eye tracking studies on acute alcohol consumption is to establish a standardized implementation/measure of alcohol intoxication in experimental designs. Indeed, the main limit associated with available studies, as fully described in Supplementary Table 2, is the high variability in the alcohol dose administration procedure, resulting in very heterogeneous BAC levels across participants. Alcohol intoxication procedure could be standardized through the use of more elaborated alcohol dose computation. Several adaptations of the classical Widmark formula (Widmark, 1932) have been proposed (e.g., Seidl et al., 2000), but there is still a difficulty to reach a non-debatable gold standard. However, a formula systematically considering the same individual parameters across participants (i.e. body weight, height, age and gender) to simultaneously take into account the 3 factors affecting the actual BAC (i.e. alcohol absorption, distribution and elimination rates)

appears as the best way to determine the dose that should be administered to reach a specific BAC level (Posey & Mozayani, 2007). The generalized use of a standardized procedure appears even more crucial since the control of the acute alcohol consumption level achieved is most often done using indirect measure. Indeed, only one study has effectively controlled BAC level through blood measures (Schmäl et al., 2000), all others studies capitalizing on the use of breathalyzer. Breath alcohol concentration measures based on the exhaled air are providing a quite reliable and easy-to-use, but yet indirect, measure of the quantity of alcohol present in participants' blood (Silva et al., 2017). As a strict BAC control through blood measure is often very difficult or unrealistic in eye tracking studies, ensuring a reliable alcohol administration procedure should constitute a priority. Moreover, the stability of the BAC level throughout the experiment should also be considered, as a high variation of this level could be observed, particularly in long-lasting designs or in settings where eye tracking calibration or inter-stimulus/inter-blocks intervals are of long duration. This control can be achieved by focusing data acquisition during the individual BAC peak period (e.g., Miller & Fillmore, 2011), by setting up a repeated alcohol administration procedure maintaining the BAC at a constant level and/or by proposing multiple BAC level assessment to consider BAC variations in data analyses.

Beyond improving the measure and evaluation of acute consumption, a basic control of the potential role played by chronic consumption on the results observed should also be conducted. Studies focusing on alcohol intoxication could thus include a measure of chronic alcohol consumption [at least the Alcohol Use Disorders Identification Test (AUDIT, Saunders et al., 1993), and ideally a Timeline Follow-Back (TLFB, Sobell & Sobell, 1992)] to exclude participants with problematic or heavy drinking pattern from their sample, or to take this variable into account. This is particularly important in view of the strong interactions observed between

acute and chronic consumption habits in available eye tracking studies (King & Byars, 2004; Miller & Fillmore, 2011; Roche & King, 2010; Schoenmakers et al., 2008).

6.2. Standardizing eye tracking measures

Beyond the critical improvements that have to be made to evaluate alcohol consumption, the main recommendation for future studies focusing on the investigation of cognitive correlates of alcohol-related disorders using the eye tracking technique is to increase homogeneity in the paradigms used across studies, and to improve the validity and reproducibility of eye tracking measurements. The determination of a standardized and reliable task dedicated to the evaluation of each specific cognitive process, together with the choice of valid eye tracking indexes, would increase the comparability across studies and the ability to infer sound conclusions regarding the cognitive abilities underlying eye movements' modifications. This standardization has already been partly accomplished regarding the investigation of attentional bias towards alcohol-related stimuli, as most studies have used the visual probe task. However, the tasks used to assess perceptive, memory and executive abilities during alcohol intoxication are characterized by a large variability in the stimuli and designs used, as well as in the eye tracking indexes reported. These strong variations across paradigms currently lead to a difficulty to compare the results reported in different studies and to infer general conclusions regarding the modification of each process following alcohol intoxication. A potential solution might be offered by recent attempts to develop more standardized paradigms measuring the processes related to eye tracking indexes. For example, the recent open-source protocol developed by Nij Bijvank et al. (2018) constitutes an interesting opportunity to carry out studies with standardized procedure.

This protocol indeed proposes 6 tasks together with automated methods to measure and analyze eye movements. Among these tasks, perceptive abilities can be assessed through the fixation task, the horizontal prosaccades task and the express task, working memory through the double-step saccadic task and inhibition through the antisaccade task. This initiative should encourage other ones and it appears particularly interesting to develop different modules within this kind of protocols, targeting specific cognitive processes. This standardization of the paradigms should also be accompanied by a clarification of the eye tracking indexes to be reported. Indeed, the current literature is characterized by a large variability of the reported indexes (e.g., saccade latency/orientation, initial fixation, number of fixations, dwell time) but also of the interpretation related to each index (e.g., initial fixation is alternatively considered as an index of early perceptual processing, as related to the automatic capture of attentional resources, or even as reflecting more high-level executive processes). The establishment of gold standards determining the best paradigm and eye tracking indexes to measure each cognitive process would thus allow a better understanding of the underlying processes and of the alterations specifically associated with alcohol intoxication.

7. Conclusion

The present systematic review encompassed all eye tracking indexes (i.e. saccade amplitude, latency, velocity, gain, initial fixation, number of fixations, dwell time, as well as more innovative measures) exploring all cognitive processes (i.e. perceptive/motor abilities, attentional bias, memory, executive functions, prevention messages processing) in all studies exploring acute alcohol consumption in humans. This integrative synthesis led to the main conclusion that alcohol intoxication is centrally associated with

decreased oculomotor accuracy/speed and reduced memory/executive functions performance. Moreover, while eye tracking measures have clearly documented a robust attentional bias following alcohol intoxication, the interactions between acute and chronic alcohol consumption regarding this bias remain to be clarified. Finally, even in the absence of acute alcohol intoxication, the visual attention dedicated to prevention messages is very low and these messages appear to have a very limited impact, if any, on actual consumption. This review also underlined the current shortcomings of this field, and centrally the limits related to acute alcohol consumption measure and to the interpretation of eye tracking indexes. The identification of these limits led to the proposal of crucial perspectives for future research, to promote higher methodological standards for upcoming studies.

Conflict of interest statement

The authors declare no conflict of interest.

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Figure

Fig. 1. PRISMA flow diagram describing the selection and review process of the papers included.

Journal Pre-proof

Table 1. Description and main results of eye tracking studies on acute alcohol consumption.

Authors (year)	Population			Exclusion criteria	Exposures			Comparator		Design				Outcomes		
	Sample (N)	Age [M(sd)]	Gender ratio (% males)		Diagnosis / Characteristics	Alcohol measure	Comorbidities	Control group	Matching variables	Processes measured	Task	Stimuli	Eye tracking indexes	Main results	Limitations	Key conclusions
Childs et al. (2012)	13	26.9 (1.1)	53%	Substance dependence Serious medical condition High blood pressure Abnormal EEG	>5 cigarettes/day >0 binge episode/week [>4 (men) or >3 (women) doses on	Adapted SCID Drinking days/month Doses/drinking day Binge episodes in last 30 days	None (within-subject design) Alcohol intoxication Other drug use Sobriety	None	Automatic (prosaccade) and controlled (antisaccade, pursuit) eye movements	Saccade task Smooth pursuit task	Still (saccade task) or moving (smooth pursuit) targets	Gain (participant's eye velocity compared to target's velocity) Saccadic latency, velocity, accuracy	No effect of low intoxication (0.4g/kg) Impaired gain and higher saccadic latency during high intoxication (0.8g/kg) Deficits partly compensated by varenicline	Limited sample size Single dose of varenicline Focus on heavy drinkers	Varenicline (2 mg) reduces the eye movements deficits induced by high intoxication (0.8g/kg)	

				BMI <19 or >26 Age <21 or >45 Pregnancy/Lactation Alcohol/drug consumption 24 hours before testing	one occasion]											
Ellert et al. (2014)	171	NR	50%	None	NR	NR	NR	Between n-subject design: 81 intoxicated 90 sober	NR	Attention to advertisements	Free visual exploration	5-minute video of a football match with advertisements	Time to first fixation Number of fixations Dwell time	Reduced number of fixations but increased dwell time on advertisements during sport programs Increased recall of advertisement's brands during intoxication	No BAC measure No measure of chronic consumption No control of biasing variables No group matching	Alcohol intoxication reduces the number of fixation but increases dwell time and memory encoding of advertisements

Fernie et al. (2012)	52	21.2 (2.8)	49%	Alcohol dependence Drugs interacting with alcohol consumption Age <18 or >30 No drinking occasion (>5 drinks) in the last 14 days Pregnancy	Heavy drinkers (>21 (men) or >14 (women) doses/week] Moderate drinkers (<22 (men) or <15 (women) doses/week]	TLFB AUDIT AAAQ Desires for Alcohol Subjective intoxication scale	NR	26 heavy drinkers 26 moderate drinkers	Age Gender	Attentional bias towards alcohol-related cues	Visual probe task	10 alcoholic beverage images 10 matched objects images	Dwell time	No behavioral attentional bias in moderate/heavy drinkers Higher dwell time towards alcohol-related cues in heavy (independent of intoxication level) and light (only during low intoxication) drinkers	Alcohol consumption measured on two last weeks Weak distinction between light and heavy drinkers No control of biasing variables	Attentional bias (higher dwell time for alcohol-related stimuli, without difference at behavioral level) in heavy drinkers is not modified by intoxication This attentional bias is only present during intoxication in moderate drinkers.
Field et al. (2005)	19	21.6 (2.9)	37%	Alcohol-related problems Non-daily smokers Alcohol consumption	NR	Desires for Alcohol Desire to drink	NR	None (within-subject design)	None	Attentional bias towards smoking cues	Visual probe task	20 smoking-related images 20 matched	Initial fixation Dwell time	Increased dwell time towards smoking-related cues during intoxication (0.4g/kg), without change in initial fixation	Limited sample size Low control on chronic consumption No dissociation between	Alcohol intoxication reinforces the attentional bias towards smoking-related cues in smokers

				<10 drinks/week No binge episode during the last 30 days Body weight <50kg (women) or <60kg (men)							non- smoking related images		psychological and pharmacological effects			
Frings et al. (2018)	92	23.7 (6.6)	20%	NR	NR	AUDIT	NR	Between n- subject design (4 conditio ns): bar/cl assical	NR	Attention to alcohol prevention message s	Free visual explora tion	One alcohol- related prevention poster One health- related poster	Number of fixations Dwell time	Reduced number of fixations and dwell time for alcohol-related poster (compared to health-related poster) in bar (but not in classical) laboratory No influence of alcohol- related poster on alcohol consumption	Basic posters in terms of message and visual characteristics Focus on heavy drinkers No control of biasing variables No group matching	The attention dedicated to prevention posters is reduced in alcohol-cue rich environments

							laboratory X									
							alcohol/health related poster									
Harvey (2014)	32	23 (6)	28%	Alcohol consumption contra-indication No binge episode during the last 90 days	NR	NR	NR	None (within-subject design)	None	Exploration/memory encoding of faces	Free visual exploration	10 same-race male faces 10 other-race male faces	Number of fixations/dwell time on face parts Visual scanning (saccadic distance)	No influence of intoxication on face encoding Reduced face scanning and number of fixations during intoxication Increased dwell time on nose and reduced dwell time on eyes during intoxication	Strong variations in BAC level No control of biasing variables Low control on chronic consumption	Alcohol intoxication changes visual scanning of faces (increasing the nose/eyes focus ratio), without impacting memory encoding
Harvey et al. (2013a)	120	19.7 (2.7)	35%	Alcohol consumption	NR	NR	NR	Between-	Age Gender	Exploration/memory	Free visual	5 images of an individual	Peripheral/central	No influence of intoxication on visual	Strong variations in BAC	Alcohol intoxication does not influence visual exploration and memory

				contra- indication No binge episode during the last 90 days				subject design: Alcohol intoxica tion Sobriet y		encoding of complex scenes	explora tion in various contexts	number of fixations Peripheral /central dwell time	exploration of complex scenes No influence of intoxication on identification and memory of complex scenes Reduced memory self- confidence without increased memory suggestibility during intoxication	No control of biasing variables Low control on chronic alcohol consumption	encoding of complex scenes	
Harvey et al. (2013b)	106	21.7 (4.4)	24.5 %	Alcohol consumption contra- indication No binge episode during the last 90 days	NR	NR	NR	Between- subject design: Alcohol intoxica tion	Age Gender	Explorati on/memo ry encoding of complex scenes	Free visual explora tion	One emotional ly salient scene One neutral scene	Number, amplitude and velocity of saccades Peripheral /central	No influence of intoxication on number, amplitude and velocity of saccades Increased number of fixations and dwell time on the central features	Only two pictures used Strong variations in BAC level No control of biasing variables	Alcohol intoxication changes visual exploration of complex scenes by increasing the attentional focus on central features, globally reducing memory encoding

								Sobriety					number of fixations	of visual scenes during intoxication	Low control on chronic consumption	
King & Byars (2004)	34	28.6 (0.7)	76%	Substance dependence Current/past psychiatric or medical disorder Pregnancy	Heavy drinkers (>9 doses/week) >0 binge episode/week [>4 (men) or >3 (women) doses on one occasion]	B-MAST Drinking days/week Doses/drinking day Binge episodes in last 180 days	Personality, affective sensation seeking measures	20 heavy drinkers 14 light drinkers	Age Gender Personality, affective sensation seeking measures	Automatic (prosaccade) and controlled (smooth pursuit) eye movements	Saccade task Smooth pursuit task	Still (saccade task) or moving (smooth pursuit) white dots	Saccadic latency and velocity (saccade task) Time on target (smooth pursuit)	Unchanged eye movements during low intoxication (0.4g/kg) Reduced time on target and saccadic velocity but increased saccadic latency during high intoxication (0.8g/kg) Low influence of chronic consumption on acute effects regarding eye movements	Small sample Mostly male participants	High alcohol intoxication impairs smooth pursuit and saccadic latency/velocity, independently of chronic consumption

					Low social drinkers (<5 doses/week)											
Lamers & Ramaekers (2001)	16	23.6 (2.9)	50%	Substance dependence Psychiatric, medical or neurological disorder Limited driving experience Psychoactive medication Pregnancy	Regular alcohol/marijuana consumers	Doses/week	NR	None (within-subject design) 4 conditions: alcohol, marijuana, both or none	None	Visual scanning while driving	Driving test	Real-life driving situation	Number of visual scans at road intersections	Unchanged visual scanning and driving performance during alcohol or marijuana intoxication Slightly reduced visual scanning during combined alcohol/marijuana intoxication	Small sample No measure of chronic consumption Limited use of eye tracking indexes	Mild alcohol intoxication does not modify visual scanning during car driving

Ma et al. (2011)	16	18.1 (1.4)	100%	Regular consumption of alcohol, caffeine, nicotine	NR	NR	NR	None (within-subject design)	None	None	None	None	Pupillary diameter	Increased pupillary diameter at short term (1hour) during high intoxication (1g/kg) Decreased pupillary diameter at mid-term (24 hours) during high intoxication (1g/kg)	Small sample Only male participants No control of biasing variables Low methodological quality	Alcohol intoxication increases pupillary diameter
Marinkovic et al. (2013)	22	24.8 (2.5)	50%	Psychoactive medication Health-related disorder	Light/moderate drinkers	B-MAST	NR	None (within-subject design)	None	Automatic (prosaccade) and controlled (antisaccade) eye movements	Saccade task	Grey dots	Saccadic latency	Increased antisaccade latency in intoxication, indexing impaired conflict processing Reduced anterior cingulate activation following errors during intoxication	Low control on chronic consumption No control on biasing variables	Alcohol intoxication reduces anterior cingulate activation in saccadic conflict, lowering inhibitory control and increasing antisaccade latency

Marks et al. (2015)	20	40.5 (6.1)	50%	No use of cocaine/alcohol in the last 30 days Serious medical, neurological or psychiatric condition No recent other drug use Pregnancy	NR	MAST Doses/week	NR	None (within-subject design)	None	Attentional bias towards cocaine-related cues	Visual probe task	10 cocaine-related images 10 matched object images	Dwell time	No behavioral attentional bias towards cocaine in cocaine users. Higher dwell time towards cocaine-related cues, independent of intoxication level	Low control on chronic consumption No control on biasing variables Mixing alcohol-dependent, alcohol abusers, and light drinkers No control group	Alcohol intoxication increases cocaine craving without influencing cocaine-related attentional bias (increased dwell time) in cocaine users
Marple-Horvat et al. (2008)	10	24.8	50%	Limited driving experience	NR	NR	NR	None (within-subject design)	None	Oculo-motor coordination	Simulator or car driving	Virtual countryside road	Cross-correlations between horizontal eye movements and	Reduced eye movements speed during alcohol intoxication Reduced eye-steering coordination, correlated with alcohol intoxication level and leading to	Low sample size Low control on chronic consumption No control of biasing variables	Alcohol intoxication reduces the coordination between eye and motor movements, leading to lower driving performance

												steering movements	reduced driving performance	Limited use of eye tracking measures		
Masimore & Spilich (2001)	20	18-22	25%	Heavy drinking	Moderate drinkers	NR	NR	Between-subject design: 10 intoxicated 10 sober	Age Gender Drinking habits	Control of visual scanning while driving	Free exploration	4 driving scenes	Number of fixations Dwell time	Reduced number of fixations on pertinent parts of driving scene (without dwell time difference) during alcohol intoxication Reduced visual exploration during mild intoxication	Low sample size Low control on chronic consumption No control of biasing variables Limited number of uncontrolled stimuli	Alcohol intoxication reduces the number of fixations on the important features of a driving scene, without modifying dwell time
Miller & Fillmore (2011)	20	22.8 (2.6)	65%	Alcohol dependence Recent drug use	Frequent drinkers (>1 drinking occasion/month, >1 dose/occasion)	B-MAST	NR	None (within-subject design)	None	Attentional bias towards alcohol-related cues Saccadic efficiency	Visual probe task	10 alcoholic beverage images 10 matched soft drink images	Saccadic accuracy and velocity Dwell time	No behavioral attentional bias in heavy drinkers, whatever the intoxication level Higher dwell time towards alcohol-related cues among heavy	No control group Small sample No control of biasing variables	The attentional bias (higher dwell time for alcohol-related stimuli, without difference at behavioral level) in heavy drinkers is not modified by alcohol intoxication

													drinkers, whatever the intoxication level		Alcohol intoxication reduces saccadic velocity and accuracy in heavy drinking	
													Linear decrease of saccadic accuracy/velocity with intoxication increase			
Moss et al. (2015)	56	22.3 (2.2)	55%	AUDIT>21	NR	AUDIT	NR	Between-n-subject design: Alcohol intoxication Sobriety	Age Gender AUDIT	Attention to alcohol prevention messages	Image content recall	5 alcohol-related prevention posters 5 health-related posters	Initial fixation location Dwell time	Initial fixation on positive/negative imagery rather than on prevention message for alcohol-related poster Higher dwell time for positive/negative imagery than for prevention message for alcohol-related poster Lower dwell time on prevention message for alcohol-related than health-related posters	Posters focused on responsible drinking rather than on drinking reduction Absence of matching between alcohol-related and health-related posters	Low visual attention is dedicated to prevention messages in posters promoting responsible drinking Such posters might increase alcohol consumption

Nawrot et al. (2004)	15	24	60%	Problem drinking Family history of alcohol-dependence Serious medical condition BMI <20 or >30 Age<21 Visual impairments Pregnancy	NR	NR	NR	None (within-subject design)	None	Depth perception Smooth pursuit Compensatory eye movements	Binary choices on depth Pursuit task (with or without head translations)	Black dots	Gain Slow and fast (saccadic) eye movements Motion parallax and stereopsis thresholds	Reduced accuracy of slow eye movements during intoxication Increased motion parallax thresholds during intoxication Preserved binocular stereopsis thresholds during intoxication	Small sample High variations in BAC level	Alcohol intoxication impairs depth perception from motion parallax by reducing the efficiency of slow eye movement system
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Orquin et al. (2014)	Study 1: 36	Study 2: 36	Study 1: 23.9 (1.8)	Study 2: 23.0 (1.7)	Study 1: 64%	Study 2: 54.5%	NR	NR	NR	NR	NR	NR	Attention to advertisements	Free visual exploration	36 advertisements with various perceptual/conceptual load	Time to first fixation, number of fixations before first fixation, and dwell time for each part	Increased attention towards perceptual features of advertisements for forced exposure during intoxication Reduced attention to features of advertisements and reduced memory encoding for voluntary exposure during intoxication	No BAC manipulation BAC level No control of biasing variables Low control on alcohol consumption	Alcohol intoxication differentially influences attentional focus towards perceptual features of advertisement according to exposure type (increase for forced exposure, decrease for voluntary exposure)
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Roberts et al. (2014)	80	23.3 (2.4)	41%	Alcohol dependence Psychiatric disorder Age <21 or >35 Drug consumption Pregnancy	Regular/Social drinkers	TLFB B-MAST (Binge) Drinking days and number of doses in last 90 days	NR	None (within-subject design)	None	Inhibitory saccadic control Saccadic latency/accuracy	Delayed ocular response task	White circles	Number of premature saccades Saccadic latency/accuracy	Increased number of premature saccades during intoxication Increased saccadic latency and reduced saccadic accuracy during intoxication Reduced inhibitory control during intoxication, positively correlated with chronic consumption among individuals with high bias	No control group No control of biasing variables No eye tracking measure of the attentional bias	Alcohol intoxication impairs saccadic latency/amplitude and inhibitory control of saccades in social drinkers
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Roche & King (2010)	138	25.6 (0.6)	57%	Heavy drinkers (>9 doses/week) Substance dependence Current/past psychiatric or medical disorder Pregnancy Low social drinkers (<6 doses/week)	>0 binge episode/week [>4 (men) or >3 (women) doses on one occasion] B-MAST Drinking days/week Doses/drinking day Binge episodes/month	SCID	78 heavy drinkers 60 light drinkers	Age Gender BMI	Automatic (prosaccade) and controlled (antisaccade, pursuit) eye movements	Saccade task Smooth pursuit task	Still (saccade task) or moving (smooth pursuit) targets	Reduced gain and saccadic latency during low intoxication (0.4g/kg) Reduced gain and saccadic velocity/accuracy, and increased saccadic latency during high intoxication (0.8g/kg) Gain (smooth pursuit) Stronger deficit in prosaccadic latency, accuracy and velocity in light drinkers (compared with heavy drinkers)	Small sample Mostly male participants	High alcohol intoxication is associated with global eye movement impairment, which are partly observed in low alcohol intoxication A partial reduction of these impairments is observed in heavy drinking
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Roche et al. (2014)	104	24.9 (0.2)	62.5 %	Substance dependence Current/past psychiatric or medical disorder Pregnancy BMI <19 or >30 Age <21 or >29	Heavy drinkers (>9 and <41 doses/week) >0 binge episode/week [>4 (men) or >3 (women) doses on one occasion]	TLFB Quantity-Frequency Interview Drinking days /month Doses/drinking day Binge episodes /month Maximum doses/occasion	SCID	104 heavy drinkers from a previous cohort	Age Gender Education BMI Familial history of alcoholism	Automatic (prosaccade) and controlled (antisaccade, smooth pursuit) eye movements	Saccade task Smooth pursuit task	Still (saccade task) or moving (smooth pursuit) targets	Saccadic latency, accuracy and velocity (saccade task) Gain (smooth pursuit)	Impaired gain, prosaccade latency/velocity, and antisaccade latency/accuracy during high intoxication (0.8g/kg) Preserved prosaccade accuracy/antisaccade velocity during high intoxication (0.8g/kg)	No control group No low alcohol intoxication condition	The pattern of eye movement impairments observed during high alcohol intoxication in heavy drinkers is robust and reproducible
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Romano et al. (2017)	14	31.4 (7.3)	67%	Neurological disorder	NR	NR	NR	None (within-subject design)	None	Gaze-holding	Horizontal pursuit of flashing light	Flashing red light	Eye-drift velocity at various eccentricities	Increased eye-drift velocity (faster centripetal drifts, increasing with eccentricities) during intoxication Reduced gaze angle at which the nystagmus appears	Small sample No control of biasing variables	Alcohol intoxication impairs the eye movements related to cerebellar function
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Rose et al. (2013)	64	23.5 (6.5)	37%	Alcohol dependence History of psychiatric, medical or substance use disorders	NR	TLFB AUDIT Desire for drinks	NR	Between subject design: Devaluation (N=32) Non-devaluation (N=32)	Age Gender AUDIT Weekly consumption	Impact of alcohol devaluation on attentional bias towards alcohol-related cues	Concurrent choice task	Images of alcoholic / soft beverages	Initial fixation Last fixation before choice Dwell time	Decreased alcohol preference after alcohol devaluation Reduced eye tracking indexes of attentional bias (initial fixation, last fixation, dwell time) after alcohol devaluation Only partial mediation of attentional bias on alcohol devaluation's impact on alcohol preference	No control of biasing variables Mixing between intoxication and alcohol devaluation effect	Alcohol devaluation procedure reduces alcohol-related attentional bias
Rose et al. (2018)	60	22.3 (4.2)	53%	Substance dependence Medical/psychiatric disorder Medication	Regular drinkers	TLFB AUDIT Alcohol urge	NR	Between subject design:	Age Gender AUDIT	Impact of alcohol devaluation on attentional bias towards	Multi-phase concurrent choice task	Images of alcoholic / soft beverages	Initial fixation Dwell time	Reduced eye tracking indexes of attentional bias (initial fixation, dwell time) after alcohol devaluation	No control of biasing variables Mixing between intoxication and alcohol devaluation effect	Alcohol devaluation procedure reduces alcohol-related attentional bias

				Pregnancy		Doses/week		Devaluation (N=28)	Weekly consumption	alcohol-related cues				Full mediation of attentional bias on alcohol devaluation's impact on cue-elicited choices, and partial mediation on alcohol devaluation's impact on goal-directed choices		
								Non-devaluation (N=32)	Weekly binge episodes							
Schmäl et al. (2000)	12	27.7	83%	History of neurologic, ophthalmologic, or metabolic disease Medication "Non moderate" drinking	NR	NR	NR	NR	NR	Dynamic visual acuity	Target fixation during body oscillations	Snellen Pflüger optotypes	Vertical eye movements Phase shift (body/eye movement's lag)	Increased amplitude of vertical eye movements (eyes closed) during body oscillations after intoxication Increased phase shift and decreased dynamic visual acuity (eyes opened) during body oscillations after intoxication	No control of chronic consumption No control of comorbidities	Alcohol intoxication decreases oculomotor response following body movement

Schmitt et al. (2013)	40	30.8 (11.0)	60%	Medical condition Pregnancy	NR	NR	NR	Comparison with database	Age	Automatic (prosaccade) eye movements Pupillary reaction	Saccade task	Still targets	Saccadic latency, velocity and accuracy Saccade main sequence (relationship between peak velocity of saccadic eye movement and corresponding eye displacement) Reduced saccadic velocity and accuracy during intoxication No influence of intoxication on eye movement variables	Unmatched control group High variations in BAC levels No control of biasing variables	Saccadic movements cannot differentiate low alcohol intoxication from soberness
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Schoenmakers et al. (2008)	22	20.3 (2.2)	55%	NR	Heavy drinkers (>21 (men) or >14 (women) doses/week]	TLFB AUDIT Desires for Alcohol Subjective intoxication scales	NR	None (within-subject design)	None	Attentional bias towards alcohol-related cues	Visual probe task	14 alcohol-related scenes 14 matched non-alcohol related scenes	Initial fixation Dwell time	No difference in initial fixation and dwell time between alcohol-related pictures and non-alcohol related pictures among heavy drinkers in the placebo condition Increased initial fixation and dwell time towards alcohol-related cues among heavy drinkers during intoxication (0.4g/kg) Correlation between behavioral and eye tracking indexes of bias during intoxication	No control group Small sample Low control on chronic consumption No control of biasing variables	Alcohol intoxication is associated with an attentional bias towards alcohol-related cues in heavy drinkers, this bias being absent during sobriety
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Silva et al. (2017)	20	22.9 (6.1)	55%	Reduced visual abilities Psychiatric/neurological disorder Alcohol dependence Family history of alcohol-related disorders Drug consumption Pregnancy	Moderate drinkers	AUDIT Consumption duration/frequency Doses /occasion	Depression Anxiety	None (within-subject design)	None	Strategic visual scanning	Visual maze task	Two dimension mazes	Saccadic latency Number of fixations Dwell time	Increased first saccade latency during intoxication Increased number of saccades/fixations and dwell time during intoxication Specific increase of number of fixations and dwell time on key regions during intoxication	Multi-determined task Weak links between eye tracking and performance measures Low control on chronic consumption No control of biasing variables	Alcohol intoxication increases fixations and dwell time during decision-making tasks, leading to reduced performance
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Vorstius et al. (2012)	30	24.1	53%	Alcohol-related disorder Medical disorder Pregnancy	Regular alcohol drinkers	B-MAST Drinking occasions/week Doses/occasion	NR	None (within-subject design)	None	Saccadic accuracy/velocity Saccadic reprogramming	Double-step task	Grey circles at various eccentricities	First saccade latency/amplitude/velocity Reprogramming time (i.e. first saccade latency minus inter-stimulus interval) Between-step latencies (lag between	Increased saccade latency and reduced saccade velocity during intoxication Increased time to cancel the first saccade and adjust saccade amplitude during intoxication	Low control on chronic consumption No control of biasing variables	Alcohol intoxication impairs saccadic speed and saccade reprogramming abilities in a double-step paradigm
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Weafer & Fillmore (2013)	40	23.4 (2.6)	55%	Substance use disorder Neurological/medical disorder	Heavy drinkers (>9 doses/week) TLFB B-MAST Desire for alcohol >0 binge episode/week [>4 (men) or >3 (women) doses on one occasion] Low social drinkers (<5 doses/week)	20 heavy drinkers 20 light drinkers	NR	Gender BMI	Attentional bias towards alcohol-related cues	Visual probe task	10 alcoholic beverage images 10 matched soft drink images	Dwell time	Attentional bias (dwell time towards alcohol-related cues) among heavy drinkers during sobriety, correlated with chronic consumption Linear decrease of attentional bias with intoxication increase in heavy drinkers Stable and moderate attentional bias in light drinkers	Limited control on chronic consumption No control of biasing variables No report of behavioral correlates of attentional bias Focus on dwell time	Alcohol intoxication reduces attentional bias in heavy drinkers, which remains stable in light drinkers
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Legend: AAAQ, Approach and Avoidance of Alcohol Questionnaire (McEvoy et al., 2004); AUDIT, Alcohol Use Disorders Identification Test (Saunders et al., 1993); (B-)MAST, (Brief) Michigan Alcohol Screening Test (Pokorny et al., 1972); NR, Not Reported; SCID, Structured Clinical Interview for DSM-IV; TLFB, Timeline Follow-Back (Sobell & Sobell, 1992)