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The sensitivity of laboratory tests assessing driving related skills to dose-related impairment of alcohol: A literature review

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ABSTRACT

Laboratory tests assessing driving related skills can be useful as initial screening tools to assess potential drug induced impairment as part of a standardized behavioural assessment. Unfortunately, consensus about which laboratory tests should be included to reliably assess drug induced impairment has not yet been reached. The aim of the present review was to evaluate the sensitivity of laboratory tests to the dose dependent effects of alcohol, as a benchmark, on performance parameters. In total, 179 experimental studies were included. Results show that a cued go/no-go task and a divided attention test with primary tracking and secondary visual search were consistently sensitive to the impairing effects at medium and high blood alcohol concentrations. Driving performance assessed in a simulator was less sensitive to the effects of alcohol as compared to naturalistic, on-the-road driving. In conclusion, replicating results of several potentially useful tests and their predictive validity of actual driving impairment should deserve further research. In addition, driving simulators should be validated and compared head to head to naturalistic driving in order to increase construct validity.

1. Introduction

Many individuals are prescribed psychoactive drugs to relieve symptoms related to mental, sleep or other disorders. A major problem associated with the use of these drugs may be daytime sleepiness and associated impairment of psychomotor functioning during the day, which could adversely affect daily activities, such as automobile driving. The effects of psychoactive drugs on driving have been widely established by either epidemiological or experimental study designs (for reviews see Dassanayake et al., 2011; Elvik, 2013; Mailis-Gagnon et al., 2012; Vermeeren, 2004; Verster et al., 2004). It has been recognized that a standardized behavioural assessment should be part of a structured, standardized protocol for assessing drug induced driving impairment (ICADTS, 1999; Kay and Logan, 2011; Ogden and Moskowitz, 2004; Vermeeren et al., 1994; Walsh et al., 2008).

Driving is a highly complex activity involving a wide range of cognitive, perceptual, and motor activities. The assessment of drug effects on a wide range of relevant driving skills has been advised to progress from laboratory and driving simulator tests, during initial screening, to on-the-road driving tests as the final assessment (ICADTS, 1999). Laboratory tests are generally a first step to screen for a drug's impairing potential in early phase clinical trials, as these tests are cost-effective, easy to administer, and widely available. Tests for initial screening should meet five criteria to be included in clinical trials assessing the effects of drugs on driving. Tests should (a) be standardized, (b) be sensitive to the potential impairing effects of drugs, (c) have established reliability (i.e. consistent results within and across studies), (d) have validity supported by theoretical models of driving behaviour (e.g. Michon, 1985) and (e) be calibrated by benchmark drugs and doses to ensure comparability of results from various research settings. Driving stimulators and on-the-road driving tests should be included in a later stage in clinical trials specifically intended to assess the drug's impairing effects on driving, as these tests have higher external validity (ICADTS, 1999; Kay and Logan, 2011; Vermeeren et al., 1994; Walsh et al., 2008). The problem for initial screening is, however, that it has not been clearly indicated which laboratory tests are most sensitive to detect drug induced impairment and consensus about which laboratory tests should be included to reliably assess drug induced impairment has not yet been reached.

A benchmark drug can be used for assessing the sensitivity of laboratory tests to drug induced impairment. A benchmark drug is a drug with known impairing effects on driving performance. Alcohol is by far the best documented substance which induces

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driving impairment. Alcohol has a clear exponential dose-dependent relationship with accident risk (Borkenstein, 1964; Krüger, 1990; Blomberg et al., 2009) and legally well-accepted criteria for driving under the influence have been established (Brookhuis et al., 2003). Alcohol is considered to be a central nervous system (CNS) depressant and has rather nonspecific effects. At low or moderate doses, alcohol acts primarily as an agonist at the $GABA_A$ receptor, but has also a direct or indirect effect on other neurotransmitter systems, such as glutamate, dopamine, opioids, and serotonin (Chastain, 2006; Vengeliene et al., 2008). This can explain the wide spectrum of impairing effects on performance, which makes it a suitable benchmark drug to assess sensitivity of tests to detect impairment.

A number of reviews have previously been published on the effects of alcohol on cognition and performance (Ferrara et al., 1994; Holloway, 1995; Krüger, 1993; Levine et al., 1975; Moskowitz and Robinson, 1988; Moskowitz and Fiorentino, 2000). The main aim of these reviews was to establish the effects of alcohol on cognitive domains per se. Nevertheless, these reviews provided some type of tests could be suitable to assess driving impairment. They indicated that sensitivity to alcohol impairment was greater in driving tests (e.g. on-the-road and simulated driving) and tests assessing controlled performance (e.g. divided attention and eye–hand coordination) compared to tests assessing automatic performance (e.g. easy tracking and simple and choice reaction time) (Krüger, 1993; Holloway, 1995). In addition, Ferrara and colleagues (1994) indicated that type of tests assessing complex psychomotor performance is required to establish alcohol induced impairment. The most recent review (Moskowitz and Fiorentino, 2000) showed that on-the-road, simulator tests, divided attention paradigms, and measures of drowsiness were most sensitive to low doses of alcohol. Vigilance, tracking, perception, visual functioning and cognitive tests were only sensitive to higher doses of alcohol. However, limited information was provided regarding specific useful tests within the domains related to driving, although it was advised not to use the critical flicker fusion and a simple reaction time test (Moskowitz and Fiorentino, 2000).

Another review recommended the use of several types of tests to assess impairment (Koelega, 1995). In that review it was argued that both vigilance (i.e. automatic behaviour) and divided attention paradigms (i.e. controlled behaviour) should be part of a test battery in assessing impairment. The use of the digit symbol substitution test, critical flicker fusion, digit span, simple and choice reaction time tests was questioned based on a lack of validity and sensitivity of these tests to the effects of alcohol. Again, limited information was provided regarding specific useful tests within driving related domains.

Selection of laboratory tests should be guided by the extent to which the scientific literature supports their ability to detect effects of a benchmark drug, such as alcohol. The aim of the present review was to evaluate the sensitivity of laboratory tests to the dose dependent effects of alcohol, as a benchmark, on performance parameters within five domains of driving related skills. More specifically, we aimed to determine which tests within driving related domains show robust sensitivity to the impairing effects of a low, moderate and high blood alcohol concentration (BAC) on performance over multiple studies.

2. Methods

The literature search was limited to the effects of alcohol on objective measures of skills related to driving performance in experimental studies between 1999 and 2014. This review updates the results of the last review of alcohol on cognitive domains (Moskowitz and Fiorentino, 2000). However, the primary focus is not to assess the effects of alcohol on cognitive domains per se, but to assess the sensitivity of specific laboratory tests to assess impairment induced by alcohol. Using various search engines (i.e. PsychInfo, Medline, and Pubmed) a broad computer search reporting the effect of alcohol on driving related skills was conducted. Search terms were 'alcohol or ethanol' and 'actual driving', 'simulated driving', 'alertness', 'arousal', 'attention', 'processing speed', 'reaction time', 'psychomotor performance', 'vision', and 'executive functions'. Furthermore, cross referencing was performed. The following criteria were used to evaluate the articles, based on the review of Moskowitz and Fiorentino (2000): (1) the laboratory test assessed a cognitive process related to driving (2) more than six participants were included (3) BACs were reported (4) at least one alcohol only treatment was included and (5) a control group design (i.e. cross-over design with a baseline condition or a between subject design with a control group) was used. After considering these criteria, 179 experimental studies were included.

First, the effects of alcohol in laboratory tests assessing cognitive processes related to driving are reviewed for each of the five domains of ability (i.e. the Essential Driving Ability Domains) recently indicated as essential for driving by an expert consensus group (Kay and Logan, 2011): (1) alertness/arousal, (2) attention and processing speed, (3) reaction time/psychomotor functions, (4) sensory-perceptual functioning, and (5) executive functions (Table 1). Tests are classified in the most appropriate domain according to the authors. The domains are chosen to cluster several laboratory tests together in one domain for structure purposes. In general, tests measure more than a single domain and domains can be incorporated in other domains. For example, tests of executive functioning usually include measures which also depend on speed of responding, which may in turn depend on sensory-perceptual functioning. Therefore, tests will be discussed in a broader perspective in which they assess several driving related domains.

Next, the studies assessing alcohol effects on simulated driving were summarized, as these tests are considered to have the second highest external validity and measure various driving skills in a controlled manner. Lastly, measures of actual driving were summarized, as on-the-road tests are generally considered to have the highest external validity in assessing the risk of drugs on driving performance (O'Hanlon, 1984; Verster and Roth, 2011). The sensitivity of the on-the-road driving test to alcohol was used as a reference. This provides the opportunity to compare the sensitivity of initial screening tools with the on-the-road driving test.

The alcohol effects on the dependent variables included in a study were recorded as a significant or non-significant difference from a control group or control condition at any point in time after the administration of alcohol. Several studies reached multiple BACs to assess the sensitivity of multiple dependent variables within a test. The effects of alcohol were divided into three classes (1) a low BAC ranging from 0.01 to 0.30 mg/ml, (2) a medium BAC ranging from 0.31 to 0.60 mg/ml and (3) a high BAC ranging from 0.61 to 1.0 mg/ml. These classes were based on current legal limits for driving under the influence of alcohol, i.e. 0.2, 0.5, and 0.8 mg/ml. A BAC of 0.2 mg/ml is the legal limit in several countries (e.g. Sweden) and in several countries for inexperienced drivers, i.e. drivers having a driving license for less than five years (e.g. in the Netherlands); 0.5 mg/ml is the legal limit for driving in most countries; 0.8 mg/ml is the legal limit in several countries (e.g. the United States and the United Kingdom). Finally, a ratio of significant versus non-significant findings was calculated for each variable as an index of sensitivity. The number of studies included in this ratio provides an indication of the robustness or reliability of the alcohol effects with repeated testing across separate studies. For example, standard deviation of lateral position in the on-the-road highway driving test was measured in 6 studies and significant impairment was found in all studies, indicating 100% impairment (i.e. highly