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# Working memory over a six-year period in young binge drinkers

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ABSTRACT

Adolescence and early adulthood are periods of particular vulnerability to the neurotoxic effects of alcohol. Young people with alcohol-use disorders display deficits in working memory (WM). This function is supported by the prefrontal cortex, a late-maturing brain region. However, little is known about the progression of cognitive dysfunctions associated with a binge-drinking (BD) pattern of alcohol consumption among non-clinical adolescents. The objective of this study was to analyze the relationship between BD trajectory and WM in university students. An initial sample of 155 male and female first-year university students was followed prospectively over 6 years. The participants were classified as stable non-BDs, stable BDs, and ex-BDs, according to the third item of the Alcohol Use Disorders Identification Test (AUDIT). WM was assessed using the Self-Ordered Pointing Task. Generalized linear mixed models were applied. The results showed that stable BDs committed more total perseverative errors and showed a lower WM span in the difficult blocks than stable non-BDs. Difficulties in WM span showed some improvement, whereas perseveration errors remained constant throughout the follow-ups in the stable BDs. There were no significant differences between ex-BDs and non-BDs. In conclusion, stable BD is associated with WM deficits, particularly perseverations and low WM span in demanding trials, when compensatory mechanisms may no longer be successful. The partial improvement in WM span may support the notion of a neuromaturational delay, whereas the temporal stability of perseveration deficits may reflect either neurotoxic effects of alcohol or premorbid characteristics. Abandoning the BD pattern of alcohol consumption may lead to partial recovery.



## Introduction

Alcohol is by far the most commonly used drug worldwide and is the third most important risk factor for disease (Rehm et al., 2009). Binge drinking (BD) is an increasingly prevalent pattern of alcohol consumption among European adolescents. This pattern is defined as the consumption of four or more drinks for women and five or more drinks for men in about 2 h, leading to a blood alcohol concentration (BAC) of 0.8 g/L (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2004). Recent reports indicate that BD is a common pattern of alcohol consumption in a third of European and American young people (Eurobarometer, 2010; Substance Abuse and Mental Health Services Administration [SAMHSA], 2013). BD is associated with an array of negative consequences and constitutes a major concern in many countries (Marshall, 2014).

Adolescence is a critical developmental period, which may contribute to a heightened vulnerability to the harmful effects of BD at this time (Bava & Tapert, 2010). Neuromaturational changes during this period (Rubia, 2013) lead to significant improvements in complex cognitive functions, the so-called “executive functions” such as working memory (WM) (Diamond, 2013). These higher-level cognitive functions are mainly supported by functional networks involving fronto-striatal pathways and the prefrontal cortex (PFC) (Fuster, 2001). The relative immaturity of these areas may make them particular targets for the deleterious effects of ethanol (Petit, Maurage, Kornreich, Verbanck, & Campanella, 2014).

Models of BD in adolescent animals induce frontal cortical degeneration (Crews, Braun, Hoplight, Switzer, & Knapp, 2000), neuroinflammation (Pascual, Pla, Miñarro, & Guerri, 2014), and

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reductions in myelin in the PFC (Vargas, Bengston, Gilpin, Whitcomb, & Richardson, 2014). In humans, young people with Alcohol Use Disorder (AUD) have prefrontal abnormalities at both structural (De Bellis et al., 2005; Medina et al., 2008) and functional levels (Caldwell et al., 2005; Tapert, Pulido, Paulus, Schuckit, & Burke, 2004). Likewise, population-based studies have shown that adolescent BDs have thicker cortices in left frontal regions (Squeglia, Sorg, et al., 2012), possibly indicating reduced synaptic pruning and less neurodevelopment. In a study carried out by our research group with part of this sample, BDs were found to have a larger volume of grey matter in the left middorsolateral prefrontal cortex (mid-DLPFC) than non-BDs (Doallo et al., 2014). Such brain alterations have been interpreted in terms of a neuromaturational delay related to heavy alcohol consumption during adolescence. At the functional level, increased frontal activity during performance of WM tasks has been observed in BDs (Campanella et al., 2013; Squeglia, Schweinsburg, Pulido, & Tapert, 2011; Squeglia, Pulido, et al., 2012), suggesting compensatory mechanisms and greater effort to perform the task at the same level as the non-BD counterparts.

At the neuropsychological level, WM has been one of the cognitive processes most commonly investigated in relation to young BDs (López-Caneda, Mota, et al., 2014). Three studies by the same research group (García-Moreno, Expósito, Sanhueza, & Gil, 2009; García-Moreno, Torrejón, Sanhueza, & Carrére, 2008; Sanhueza, García-Moreno, & Expósito, 2011) found that BDs performed poorly in WM tasks (Digit Span [WMS-III] and Corsi block tapping task [CBTT]). In relation to the executive processes of WM, female BDs committed more errors in the most difficult condition of the Spatial Working Memory task (Cambridge Neuropsychological Test Automated Battery [CANTAB]) and obtained lower strategy scores (Scaife & Duka, 2009; Townshend & Duka, 2005). However, other authors have not found any differences regarding number of errors in a similar test, the Self Ordered Pointing Task (SOPT) (Johnson et al., 2008; Xiao et al., 2009). Previous studies by our research group have shown that BDs had lower span in the Backward Digit test (Digit Span [WMS-III]) (Parada et al., 2012) and committed more perseverative errors in the SOPT (Mota et al., 2013; Parada et al., 2012) than non-BDs. The results with part of this sample showed that the differences in Digits Backward disappeared despite maintenance of a BD pattern of alcohol consumption during 2 years (Mota et al., 2013). This apparent improvement in verbal WM in BDs in comparison with age-matched non-BDs may be compatible with a neuromaturational lag, possibly indicating that improvements in WM efficiency that take place naturally during adolescence would occur later in BDs as a result of excessive alcohol consumption.

Despite the consistent deficits in WM, little is known about the long-term progression of such difficulties in relation to BD trajectories. A recent 8-year-long prospective study (Boelema et al., 2015) did not find any association between executive functions and BD trajectory in young adults. However, the authors used simple reaction time scores as indices of cognitive processes (e.g., WM), which may lead to poor identification of subtle difficulties (e.g., manipulation, perseveration). In a slightly different population, a 10-year-long follow-up study of adolescents with alcohol and other drug use (AOD) showed that different patterns of substance use were linked to poor verbal learning and memory, visuospatial memory, and WM over time (Hanson, Cummins, Tapert, & Brown, 2011), and heavier use was generally related to poor performance. In addition, there is a further gap in the literature in relation to whether recovery would occur after abandonment of the BD pattern of alcohol consumption in the short term, and if so, whether the ex-BDs would be able to perform at the same level as controls.

The main aim of the present study was to determine the relationship between WM and BD trajectory over a 6-year period in healthy university students with no other relevant risk factors, such as psychiatric comorbidity or family history of alcoholism. Bearing in mind that this pattern is associated with difficulties in specific WM processes (maintenance of information, manipulation, resistance to interference, etc.), we placed particular emphasis on disentangling some of these processes by considering different variables not previously analyzed. We also explored what happens when memory load increases (more items to monitor) and executive strategies are required to complement storage limits. Moreover, as our previous results showed amelioration of difficulties in the digit span task after 2 years of a stable BD pattern of alcohol consumption (Mota et al., 2013), we hypothesized that improvements in WM would be observed and would suggest alcohol-related delays in normal adolescent neuromaturational processes.

We tested the following hypotheses: 1) participants with a trajectory of stable BD will show poorer performance in high-demanding blocks (when they might not be able to compensate for their difficulties) of WM tasks than stable non-BDs, which may be consistent with a compensatory hypothesis; 2) despite maintenance of the pattern, stable BDs will show an improvement in WM over time, compatible with a neuromaturational delay in brain development; and 3) performance of this task by those participants who abandon the BD pattern of alcohol consumption will improve, and maintenance of an ex-BD pattern over time would imply further improvement.

## Material and methods

### *Participants*

The sample initially comprised 155 first-year university students (76 males and 79 females) recruited from different faculties of the University of Santiago de Compostela (NW Spain). All participants were Caucasian. Participants were selected by administration of an anonymous questionnaire in class (Caamaño-Isorna, Corral, Parada, & Cadaveira, 2008). The questionnaire included the Alcohol Use Disorders Identification Test (AUDIT) (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) and questions related to alcohol use (rate of consumption, age of onset, etc.). The classification criteria were based on the students' responses to two questions: the third item of the AUDIT (How often do you have six or more drinks on a single occasion? Never/Less than monthly/Monthly/Weekly/Daily or almost daily), and one question related to the rate of consumption (drinks per hour). Taking into account that in Spain a standard alcoholic drink is equivalent to 10 g of alcohol, six drinks consumed at a rate of more than two drinks per hour would bring the blood alcohol concentration (BAC) to 0.8 g/L or higher. This criterion defined a binge-drinking pattern of alcohol consumption in the present study. Thus, BD participants consumed six drinks on one occasion monthly or weekly and the rate of alcohol consumption was three or more drinks per hour. The non-BD group was defined as those who never consumed six drinks on one occasion (or less than monthly) and who consumed alcohol at a rate of two drinks or fewer per hour.

As the objective was to assess the trajectory of alcohol consumption, participants were classified as stable non-BDs, stable BDs, and ex-BDs (those who had abandoned the BD pattern at the second, third, or fourth evaluation). This classification criterion was strict and did not allow transitions or fluctuations in the trajectories (e.g., a non-BD participant who changed to a BD consumption at the third evaluation would be excluded from the analysis in the fourth evaluation but maintained for the previous evaluations, due to the ability of mixed models to deal with different number of participants in each evaluation). We are aware that this classification implies sample attrition over time. Therefore, to ensure that this