Published in final edited form as:

Curr Opin Psychiatry. 2013 July ; 26(4): 305–309. doi:10.1097/YCO.0b013e328361ea3c.

Executive functioning among young people in relation to alcohol use

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Abstract

Purpose of review—This article reviews recent findings regarding neurobehavioral factors which may be associated with risk for alcohol misuse, as well as those which may occur as a result of alcohol misuse during adolescence and emerging adulthood.

Recent findings—Current research extends previous findings by engaging multiple assessment methods and integrating behavioral and imaging technologies. These efforts reinforce previous findings regarding alcohol-related changes in macrostructure while demonstrating alterations in brain connectivity previously underappreciated. Longitudinal work now being reported suggests problem use during adolescence may be associated with persistent neurobehavioral aberrations.

Summary—For many years, little attention was directed to the neurobehavioral consequences of alcohol use across adolescence and emerging adulthood or to the neurobehavioral factors which might predispose youth to alcohol misuse. Recent work provides critical insights regarding the underpinnings of the deficits in executive function often observed in those at risk for alcohol dependence and those who develop alcohol use disorders. These studies suggest that, even when behavioral deficits are not evident, changes in brain connectivity and microstructure may be observed. Programmatic, longitudinal research must be conducted to determine the relevance of these alterations to use trajectories and long-term adaptation.

Keywords

alcohol; executive functions; neurobehavior; risk; youth

INTRODUCTION

Adolescence and emerging adulthood are periods accompanied by increased risk-taking, increased peer-group influence, and decreased parental control. These processes enable eventual separation from the family of origin and the development of individual identities. For many young people, they are also characterized by the initiation of regular and sometimes problematic alcohol use. Approximately 25% of youth in grades 8, 10, and 12

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Conflicts of interest

There are no conflicts of interest.

report alcohol use in the previous month and 13% report heavy episodic or binge drinking [1]. These alcohol-use patterns give rise to two critical questions. First, despite its widespread use, not all youth experience significant alcohol-related problems and relatively few sustain patterns of problematic use into and across adulthood. What individual variables may account for differential risk? Second, given the known neurotoxic effects of alcohol and the rapidly changing milieu of the adolescent/young adult brain, what are the neurobiological consequences of alcohol use during this critical developmental period? Interestingly, deficits in executive function have been noted as both a risk factor for and a consequence of alcohol misuse.

Executive functions refer to a set of neurobehavioral processes including abstraction and problem-solving, planning, response inhibition (behavioral control), and working memory. Although executive functions involve the frontal and prefrontal brain areas, their effective engagement relies on the integration of information from both subcortical and cortical areas. In the current review, we will examine recent neurobehavioral evidence directed to clarifying the interface of executive function and alcohol use in youth and young adults.

EXECUTIVE FUNCTION AS A PREDICTOR OF ALCOHOL USE/MISUSE

To directly examine this question, prospective longitudinal studies are required. Although a few notable investigations exist, these types of studies are expensive by any metric and demand sustained commitment by participants and investigators. Because a minority of drinkers meet diagnostic criteria for alcohol use disorders (AUDs), one requirement of effective prospective studies is the recruitment and retention of sufficiently large samples to allow meaningful analysis.

An alternative approach has been to focus comparisons between groups of youth who are at risk for developing alcohol-related problems and those who are less likely to develop these disorders. The primary means of assigning youth into these groups has been on the basis of the presence versus the absence of a family history (FH) of AUDs (FH+ versus FH-). In this literature, several classification systems have been applied, including a density measure which permits FH to be considered along a continuum ranging from 0 to 1 (if all relevant family members are affected). However, a simpler method considering only the presence or absence of parental AUDs has been shown to produce reliable outcomes and is the method most frequently used.

It is generally recognized that FH+ youth initiate drinking earlier, drink more heavily and are at increased risk for alcohol-related negative consequences and developing alcohol dependence over the course of their lifetimes (see [2]). It has been argued that this definition of risk may be too narrow; that is, increased risk also being connoted by other parental behavioral issues such as chronic smoking (nicotine dependence) and problem gambling. A discussion of these issues is beyond our current scope. Therefore, we will restrict our focus to those studies using FH as a risk factor for AUDs.

One of the challenges in conducting this work has been disentangling the effects of early alcohol use from the effects of FH+ status. Often studies have been conducted with youth or young adults who have already initiated regular drinking or have used FH as a classification

variable to subgroup persons meeting criteria for an AUD. Several recent published studies extended existing work and implemented designs to address this concern. Altered white matter integrity and aberrant prefrontal activity have been previously noted in FH+, alcohol-naive youth [3,4]. These provocative findings suggested that further study of brain connectivity among areas/regions particularly relevant to the conduct of effective executive functions be conducted. Herting *et al.* [5] reported such a study using functional connectivity MRI (fcMRI) in a group of alcohol-naive adolescents between the ages of 11 and 15 (mean age ~14). Approximately half of the sample was FH+ ($n = 13$) and the remainder were age-matched community controls ($n = 14$). Of particular relevance were their findings that areas of white matter compromise in the anterior limb of the internal capsule and the superior longitudinal fasciculus were correlated with reduced connectivity between bilateral lateral cerebellar regions and contralateral anterior prefrontal lobes. Given the growing appreciation of the role of the cerebellum in effective executive functions, these findings suggest critical aberrations in alcohol-naive at-risk youth. An underappreciated finding was the fact that neither brain-activation patterns using blood-oxygen-level-dependent (BOLD) imaging nor behavioral performance measures (e.g. behavioral interference, risky decision-making, face memory) distinguished the two FH groups. Additional research is needed to clarify whether the BOLD activation and performance measures would be affected if/when alcohol consumption was initiated.

Wetherill *et al.* [6] conducted a similar study focusing on a different system. They tested youth between the ages of 12 and 14 (mean age ~13); half the participants were FH+, half FH-. In addition to fcMRI and diffusion tensor imaging analysis, participants completed a test of visual working memory. The primary focus for this group was the frontoparietal connections underlying working memory. They found no performance differences between the two groups. Contrary to the work by Herting *et al.*, they failed to detect microstructural abnormalities in the white matter integrity. However, they did find group differences in connectivity, with the FH+ group showing reduced connectivity between the posterior parietal cortex and dorsal lateral prefrontal cortex relative to the FH- group. Furthermore, connectivity and performance were positively related to the FH- group, suggesting superior attentional processing capacity.

Another study which failed to demonstrate performance differences in executive function between FH+ and FH- youth was reported by Cservedi and Nagel [7]. These investigators compared risk-taking behavior and brain activation in youth between the ages of 13 and 15, with no or little substance use history. Contrary to their expectation, FH+ youth did not make less advantageous (i.e. riskier) choices. Additionally, the FH groups showed activation in common bilateral cortical and subcortical regions. However, FH+ youth demonstrated reduced activation in key areas, despite the absence of group differences on the behavioral measures. Specifically, FH+ youth as compared with the FH- youth exhibited reduced activation in the dorsal lateral prefrontal cortex and the cerebellar tonsil in the right hemisphere. Further analysis revealed that this differential response appears to be linked to a reduced activation in the dorsal lateral prefrontal area (right hemisphere) during risky decision-making for the FH+. In contrast, when overall activation patterns disregarding risk

condition were considered, FH+ youth showed increased bilateral activation in the parietal cortices.

These recent studies extend previous work by implicating compromise in the connectivity of and/or activation of essential brain systems in at-risk youth. However, it is noteworthy that performance differences between the subgroups were often absent, and the link between atypical neural activity and performance demands continued study. Supporting this call for further research is a recent study by Hanson *et al.* [8]. They examined hippocampal volumes in FH+ and FH– youth and determined the degree to which baseline measures predicted alcohol use 4 years later. Interestingly, they found no main effects for FH on either memory performance or hippocampal volume. Thus, as the authors conclude, previous findings of hippocampal volume differences in heavy-drinking youth are unlikely to be attributable to FH status. Furthermore, and of particular relevance to this review, is the fact that hippocampal volume did not predict substance use 4.6 years later.

Silveri *et al.* have published several recent papers with direct relevance to our question. In one of these, Silveri *et al.* [9] examined FH+ and FH– children and youth between the ages of 8 and 19. Using functional MRI (fMRI), they examined the BOLD response during the completion of a common behavioral inhibition/interference task. They reported greater activation in frontal-limbic areas among FH+ than FH– patients when completing the interference condition. Furthermore, FH+ density was positively related to activation in frontal areas. Importantly, the FH groups did not differ in the behavioral measures. The authors conclude that this increased activation reflects the recruitment of additional resources by the FH+ group which may enable equivalent performance.

From a conceptual perspective, one of the more important papers in the recent past is that published by Handley *et al.* [10] in 2011. These authors observe that, in discussions regarding the association between executive function and externalizing behaviors (e.g. alcohol misuse), broad statements regarding impairment in executive functions are regularly made without regard to the specific set of engaged processes. Of particular concern to these authors is the controversy surrounding the term ‘disinhibition’. This widely used term may refer to a number of traits associated with FH+ status and AUDs including behavioral undercontrol, impulsivity, and/or the inability to withhold responding. Building on their own and others’ work, they propose that risk might be better understood if disinhibition was subtyped as top-down-driven – executive disinhibition, versus bottom-up-driven – reactive disinhibition. The former subtype reflects failures in effortful or intentional inhibition, for example, inhibiting a response in go/no-go task. The latter subtype reflects inhibitory failures observed in novel or affect-laden contexts, for example, negative urgency, sensation seeking. Their complex study of FH, childhood behavioral disorders and alcohol use revealed that the two ‘types’ of disinhibitions were differentially associated with externalizing behaviors, with reactive disinhibition being more strongly associated with adolescent substance use, whereas executive disinhibition was associated with Attention Deficit Hyperactivity Disorder symptomatology. The study has noted limitations, for example, the nature of the adolescent substance use data and the measurement of trait impulsivity. However, the complexity of results reflects the need for consistent conceptual and operational definitions in study conduct and interpretation.

Finally, in this literature, substantial energy and resources are committed to the study of risk factors. However, identifying factors which connote resilience are, arguably, equally important. Resilience is sometimes used as a synonym for the effective use of refusal skills or the ability to rebound from negative circumstances. In its more complete interpretation, it refers to the ability to respond with appropriate (psychological) flexibility within a variety of contexts. Weiland *et al.* [11] studied cortical–striatal activation coupling, working memory, and substance use in a group of FH+ and FH– emerging adults (age 18–22 years) for whom resiliency measures obtained at ages 12–15 were available. Higher resiliency in early adolescence was related to later onset and lower substance use, better working memory, greater activation in the thalamus and striatal areas during the working memory task, and enhanced coupling between the thalamic and cingulate areas. Of particular importance was the finding that the high and low resilience groups did not differ in FH composition.

Conclusion

Although these findings of structural and functional deficits in FH+ youth strongly implicate a neurobiological predisposition for deficits in executive processes, it is critical that behavioral compromise is not uniformly observed. It is also not known whether these aberrations represent developmental delays as opposed to relatively permanent compromise, that is, developmental delays that might at least partially resolve if drinking is delayed or not initiated. Finally, recent work modeling the factors most closely associated with alcohol use initiation indicated that, although FH and indicators of behavioral under-control were important, they did not constitute the entire set of pertinent variables. Of perhaps no surprise to persons working with adolescents was the fact that the most powerful variable was whether the best friends of these adolescents drank [12].

EXECUTIVE FUNCTION AS A RESULT OF ALCOHOL USE/MISUSE

The vulnerability of the adolescent and emerging adult brain to the neurotoxic effects of alcohol has been increasingly appreciated. Two recent reviews [13,14] provide compelling evidence regarding alcohol-related neurobehavioral deficits. They note that alcohol use, particularly heavy episodic or binge drinking, is associated with reduced attention, poorer working memory, and reduced visual–spatial skills. It is also associated with structural and functional brain changes including reductions in frontal, parietal, temporal, and cerebellar volumes, and in white matter volume and integrity. Furthermore, brain activation patterns and connectivity have been shown to be altered.

One of the caveats in interpreting these data is the fact that youth with earlier and heavier use patterns also tend to have a positive FH. Thoma *et al.* [15] explicitly addressed the question by testing three groups of youth: healthy controls, FH+ youth without problematic use, and youth with a substance use disorder (SUD). Although their focus was on alcohol use, the high rates of comorbid marijuana use among problem drinkers led them to consider the separate and interactive effects of the two substances. They found that heavier drinking (drinks/drinking day) was related to poorer attention and executive function, regardless of marijuana use. However, frequency of marijuana use was associated with poorer memory, and FH+ individuals performed more poorly on visual–spatial tests.

Also, addressing the effects of both alcohol and marijuana use is a recent study by Lisdahl and Price [16]. These authors administered a neuropsychological battery including tests of memory, attention, psychomotor speed, verbal and design fluency, and cognitive inhibition to a sample of emerging adults (age 18–26 years). Importantly, the sample was sufficiently sized that sex differences could be explored. The analysis produced several important findings. First, marijuana use was associated with poorer psychomotor speed, sustained attention, and cognitive inhibition. Second, men were negatively affected by marijuana use to a greater extent than were women. Third, regardless of marijuana use, alcohol use independently predicted poorer delayed memory.

Unfortunately, it is unclear to what extent substance-related deficits may remit. Hanson *et al.* [17] examined three groups of youth: healthy controls, those with remitted SUDs (alcohol or other drug), and those with persisting SUDs. They found that, regardless of remission status, performance for the SUD groups declined over the 10-year study period. At year 10, greater cumulative alcohol use was associated with poorer visual–spatial construction skills and poorer verbal learning/memory. Cumulative use of marijuana or stimulants was not predictive of performance on these tests, although cumulative stimulant use was predictive of poorer visual learning/memory at year 10.

Conclusion

The use of alcohol by youth and emerging adults may have profound effects on neurobehavioral processes, impacting both structure and function. Although this period has been recognized as a vulnerable one in terms of increased risk-taking and experimentation, only recently have we come to appreciate its neurobiological vulnerability. Processes depending on effective executive functions are often compromised, but they do not represent the only areas affected. Relatively little is known about sex differences regarding the impact of use across this period and even less is known regarding the permanence of these deficits or their patterns of recovery. Finally, given the current literature, it is premature to make strong conclusions regarding the potential synergy of alcohol with other substances of abuse. Additional research directed to the study of alcohol in combination with commonly comorbid drugs such as marijuana should be a high priority.

Acknowledgments

Dr Nixon receives research funding from the National Institute on Alcohol Abuse and Alcoholism (R01 AA019802), the National Institutes of Health Clinical and Translational Science Award program (UF CTSI: UL1 TR000064), the State of Florida (Stewart-Marchman-Act Research Fund), the Florida Department of Health (Professionals Resource Network), the James and Esther King Biomedical Research Foundation, and Xhale, Inc. (Subcontract of SBIR Phase II - R43 AA017009).

REFERENCES AND RECOMMENDED READING

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 415–416).

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KEY POINTS

- Deficits in executive function are often associated with a parental history of alcohol dependence (FH+) and may contribute to the increased risk for alcohol misuse associated with such histories.
- Current neuroimaging work suggests that neural circuitry underlying executive functions may be altered in FH+ youth, even if behavioral deficits are not observed.
- Certain patterns of neural activity and connectivity may serve to protect youth from problematic drinking, although replication studies are needed.
- Youth and young adults who engage in alcohol misuse, particularly heavy episodic or binge drinking, demonstrate structural and functional aberrations in brain, as well as behavioral impairments which extend beyond executive functions *per se*.
- Additional research is needed to clarify the extent and trajectory of neurobehavioral improvement among youth and young adults recovering from alcohol use disorders.