Meta-control in adolescence – a longitudinal approach to investigate causes and consequences of alcohol use

Dissertation project M.Sc. Juliane H. Fröhner

Adolescence, as the transition from child- to adulthood, comes with numerous changes in human experience and behavior. The changes occur in every area of human living, ranging from administrative areas such as living circumstances to personal aspects such as social development. In this thesis, the focus lies on cognitive aspects of development, which can be assigned to the construct of meta-control: delay discounting during intertemporal choices and reversal learning (Goschke, 2013). Previously, both constructs have been associated with alcohol use, particularly with alcohol use disorders (e.g. MacKillop et al., 2011; Reiter, Deserno, Kallert, et al., 2016). The question of whether altered meta-control is a cause of drinking or if drinking causes alterations in meta-control remained unanswered. To investigate this cause-and-consequence question, we examined longitudinal data of adolescents at ages 14, 16, 18, and 22. This enabled us to test a reciprocal relationship between the early stages of alcohol use and meta-control. Importantly, the brain continues to mature during adolescence, and the time lag between the development of subcortical and cortical regions is thought to contribute to the "typical adolescent" impulsive and risky decision-making (Spear, 2000). Consequently, we employed functional magnetic resonance imaging (fMRI) to gain a deeper understanding of how the neural mechanisms of meta-control develop and how they correlate with alcohol use as a component of risky behavior.

During the fMRI analysis of our intertemporal choice data, we observed strong grouplevel effects but encountered low reliability at the individual level, a phenomenon known as the reliability paradox (Hedge, Powell, & Sumner, 2018). Consequently, we conducted a comprehensive reliability analysis, which is presented in Study 1 of this thesis (Fröhner et al., 2019). In conclusion, the selection of regions based on significant main effects at the group level may result in estimates that fail to reliably capture individual variance in the subjective evaluation of an intertemporal choice. To facilitate the assessment and reporting of fMRI contrast reliability in future studies, we have developed a toolbox that incorporates commonly used measures of both global and local reliability (https://github.com/nkroemer/reliability).

In Study 2, the objective was to address the cause-and-consequence question concerning delay discounting and alcohol use. This was achieved by employing latent growth

curve models (LGCM) to examine the associations between intertemporal choices, their (reliable) neural correlates, and drinking (Fröhner et al., 2022). Crucially, alcohol consumption increased in our sample over the course of the study, but it remained low-level. To summarize, adolescents with higher discounting rates at age 14 exhibited a greater increase in alcohol consumption over the subsequent eight years. Conversely, moderate alcohol consumption on average did not affect the development of discounting. A reduction in dorsolateral frontal activity during intertemporal choices was found to be associated with increased alcohol consumption at both age 16 and age 18. Furthermore, a reduction in this activity at age 16 was associated with more drinking at age 18.

In Study 3, we sought to determine whether differences in reversal learning, and its neural correlates are a cause or consequence of alcohol use (Fröhner, Waltmann, Reiter, Kräplin, & Smolka, submitted). In essence, individuals who consumed more alcohol were less likely to alter their choices after experiencing a monetary loss during task completion at age 18. Moreover, reward prediction errors elicited less medial frontal activity in more risky drinkers across all sessions. Our findings indicate that reversal learning processes and learning from negative feedback are particularly relevant for the development of later and heavier drinking patterns.

Collectively, the findings indicate that meta-control, as measured by delay discounting and reversal learning, increased during adolescence. Not surprisingly, alcohol consumption also increased, although it remained at a relatively low level in our sample. While steeper delay discounting preceded more alcohol consumption, associations between reversal learning and alcohol consumption are more prevalent during late adolescence, when participants already consume more alcohol. The imaging results indicate a reduction in activity in the frontal control areas in those who drink more. In addition to the reliability issue, other methodological factors have to be considered when interpreting the results. For example, the low alcohol consumption of our participants, while intriguing, makes investigations of individual differences challenging due to the limited between-subject variance. Future longitudinal studies should prioritize the reliability of their fMRI paradigms prior to acquisition and employ alternative study designs to address the cause-andconsequence question more effectively. For instance, recruiting adolescents with varying risk profiles for developing alcohol use disorders could enhance the study's ability to identify causal relationships.

References

- Fröhner, J. H., Ripke, S., Jurk, S., Li, S. C., Banaschewski, T., Bokde, A. L., . . . Grigis, A. (2022). Associations of delay discounting and drinking trajectories from ages 14 to 22. Alcoholism: Clinical and Experimental Research.
- Fröhner, J. H., Teckentrup, V., Smolka, M. N., & Kroemer, N. B. (2019). Addressing the reliability fallacy in fMRI: Similar group effects may arise from unreliable individual effects. *Neuroimage*, *195*, 174-189. doi:10.1016/j.neuroimage.2019.03.053
- Goschke, T. (2013). Volition in action: Intentions, control dilemmas, and the dynamic regulation of cognitive control.
- Hedge, C., Powell, G., & Sumner, P. (2017). The reliability paradox: Why robust cognitive tasks do not produce reliable individual differences. *Behavior Research Methods*. doi:10.3758/s13428-017-0935-1
- MacKillop, J., Amlung, M. T., Few, L. R., Ray, L. A., Sweet, L. H., & Munafò, M. R. (2011). Delayed reward discounting and addictive behavior: a meta-analysis. *Psychopharmacology,* 216(3), 305-321. doi:10.1007/s00213-011-2229-0
- Reiter, A. M. F., Deserno, L., Kallert, T., Heinze, H.-J., Heinz, A., & Schlagenhauf, F. (2016). Behavioral and Neural Signatures of Reduced Updating of Alternative Options in Alcohol-Dependent Patients during Flexible Decision-Making. *Journal of Neuroscience*, 36(43), 10935-10948. doi:10.1523/JNEUROSCI.4322-15.2016
- Spear, L. P. (2000). The adolescent brain and age-related behavioral manifestations. *Neuroscience* & *Biobehavioral Reviews*, 24(4), 417-463. doi:https://doi.org/10.1016/S0149-7634(00)00014-2