Kristof Geilenkotten
kristof@geilenkotten.com
09/03/2018

What can studies of brain-damaged individuals tell us about the way in which memory is organized?

Introduction

"In any well-made machine one is ignorant of the working of most of the parts – the better they work the less we are conscious of them it is only a fault which draws our attention to the existence of the mechanism at all", Kenneth Craik, The Nature of Explanation (1943) (20)

Whilst doing a literary study on brain-damage and memory it became clear to me that one aspect of brain damage and its effect on memory was well documented. And on top of that the author of this paper has personally experienced this (temporary) form of brain damage. Therefore this paper will more specifically mention the effects of alcohol on the brain and how it is responsible for so called Black outs.

How does our memory work

The Process

To explain how memories are created we will use the Atkinson and Shiffrin model (1968) depicted in Figure 1 The Atkinson Shiffrin theory (6). Basically there are 3 stages, sensory memory (which lasts a few seconds), a short-term storage that lasts from seconds to minutes depending on rehearsal, and an long-term storage that can last a healthy lifetime.

We will now mainly focus on the transfer of information from short-term memory to long-term memory, because as we will show later this is mainly impacted by the (temporary) brain damage caused by alcohol, although also other stages are in lesser extend affected by alcohol.

The likelihood that information will be transferred (encoded) to long-term memory is dependent on *rehearsal*, *the depth of processing* (i.e. true understanding of the information prior to encoding), *attention*, *motivation* and *arousal* (7).

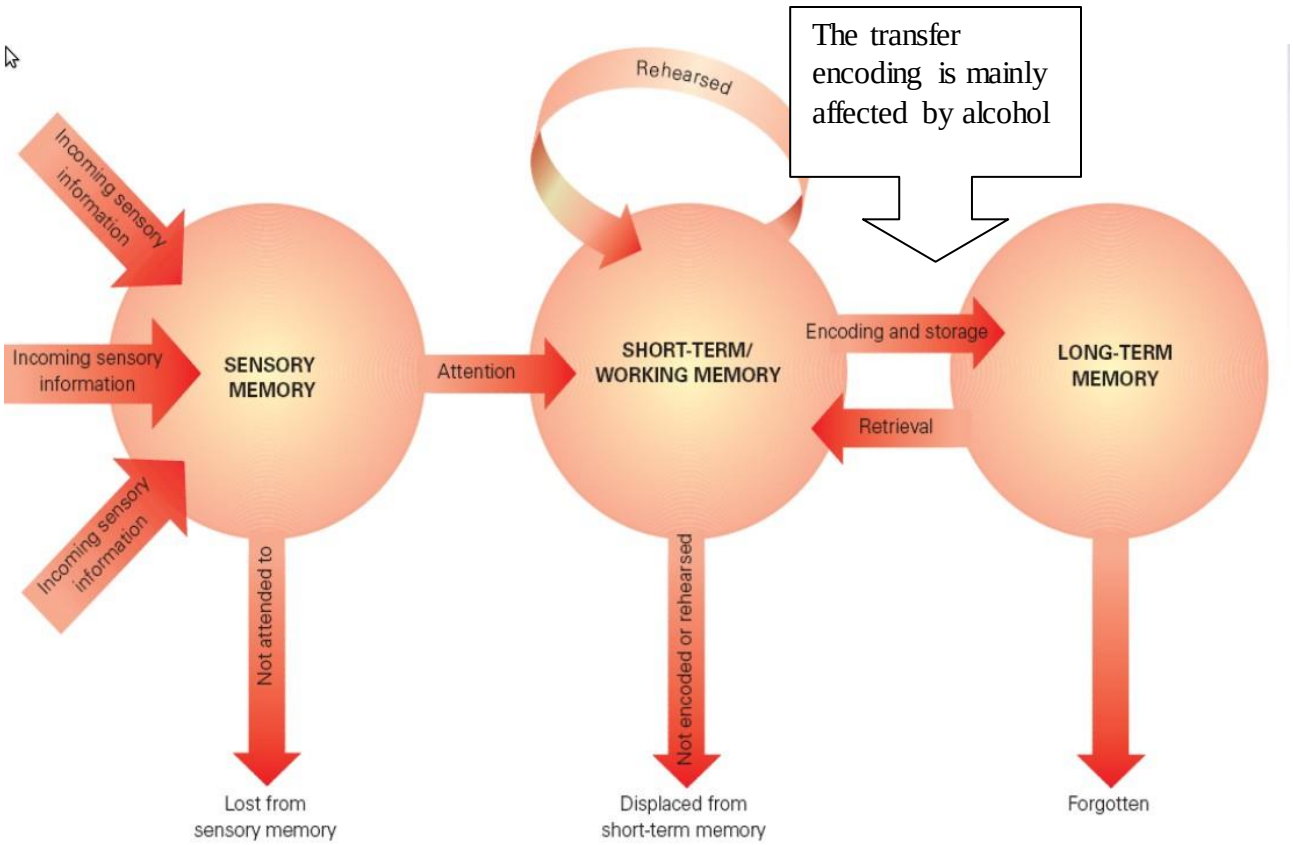

Figure 1 The Atkinson Shiffrin theory (6)

The brain

Figure 2 organization of the brain (17,16), shows the structure of the brain, and although there is interaction between almost all parts for some human functions, the part that primarily concerns memory is the hippocampus which resides in the limbic system in the forebrain.

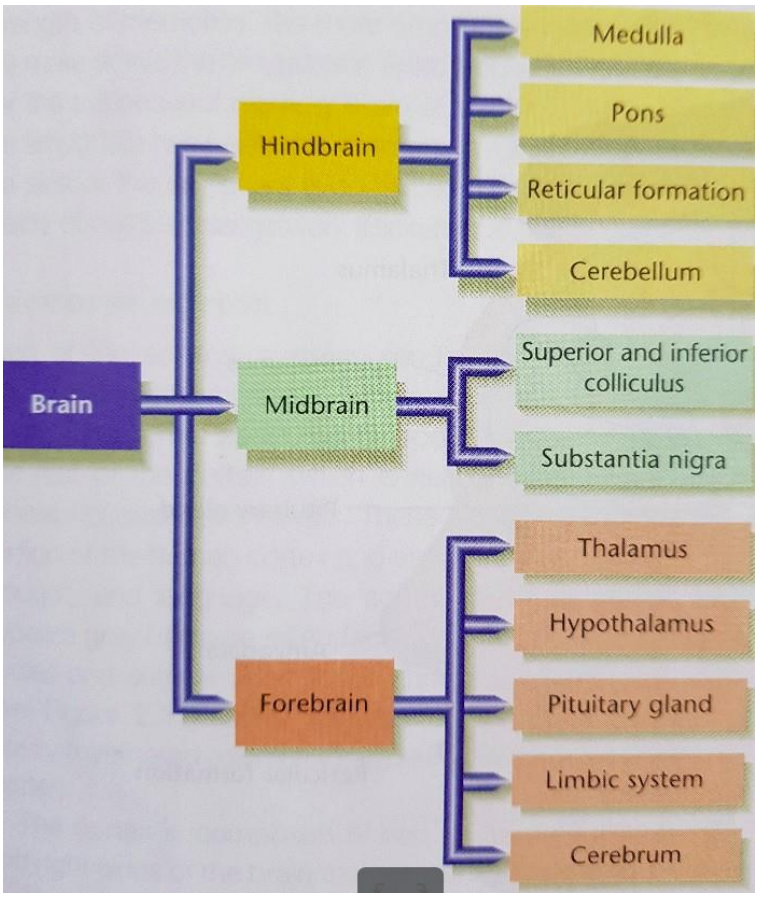

Figure 2 organization of the brain (17,16)

How sensory triggers are received through the prefrontal cortex and dispatched to the different functional parts is explained below (15, and Figure 3 Pathways of information flow in between the hippocampus and prefrontal cortex (15)).

Perceptual information about objects and events are initially processed in pathways for specific sensory modalities (vision, hearing, touch, olfaction) which project to multiple 'association' cortical areas that compose the 'what' stream of cortical processing that leads into perirhinal and lateral entorhinal cortex (blue). Information about 'where' in space events occur is processed in a separate cortical stream (including posterior parietal, retrospenial, and other cortical areas) that lead into the parahippocampal and medial entorhinal cortex (green). These streams then converge in the hippocampus. There, in the dorsal (animals) or posterior (humans) hippocampus, neural ensembles encode specific objects and the locations they occur within a context. By contrast, neural ensembles in the ventral (animals) or anterior (humans) hippocampus link events within a context and strongly distinguish between different contexts. Contextual representations from the ventral/anterior hippocampus are sent directly to the medial prefrontal cortex, which is positioned to influence the retrieval of specific object representations via its particularly strong connections to perirhinal and lateral entorhinal cortex.

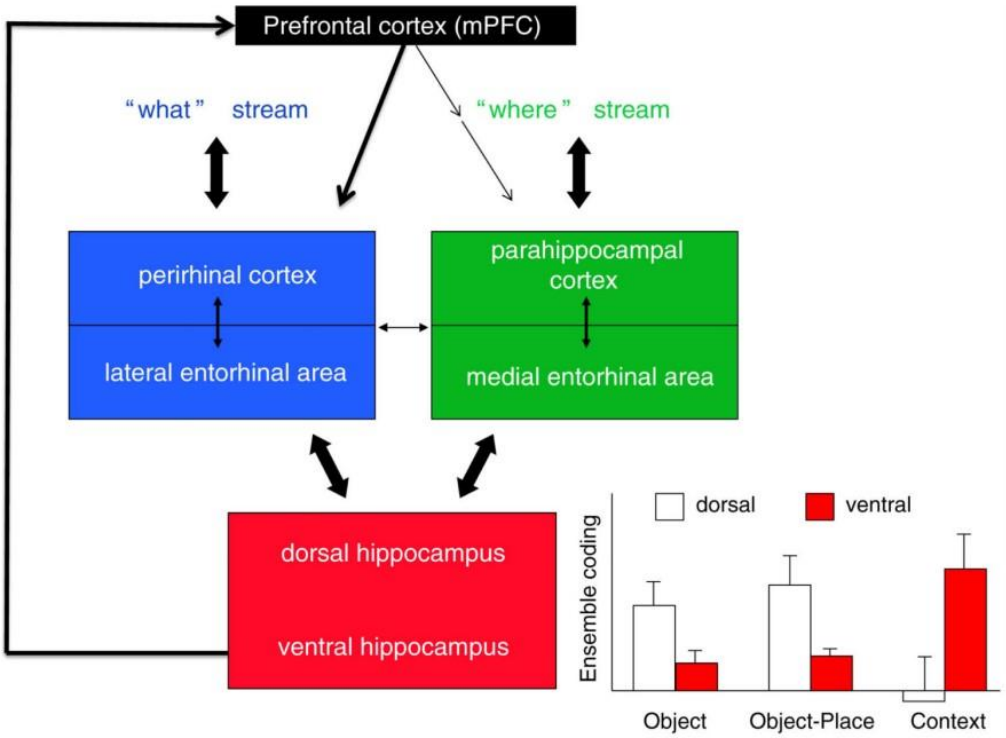

Figure 3 Pathways of information flow in between the hippocampus and prefrontal cortex (15)

The neurons and neuron transmitters

Memory and learning involves a change in neural activity. The Hebbian learning rule (8) learns us that if input from neuron A repeatedly triggers the firing rate of neuron B, the connection between A and B grows stronger which leads to a *permanent* change to the synapses between A and B.

(Temporary) damage done by alcohol and its (temporary) effect on memory

In this paper we specifically discuss the temporary damage and temporary effects of alcohol on the brain. The long-term effects on the brain have not been studied in depth but one paper checked mentioned "There were no correlations with age and any of the volume or neuron number measures. Hippocampal volume correlated with brain volume and with the regional gray and white matter volumes within the hippocampus. In addition, hippocampal gray matter volume correlated with the number of CA1 pyramidal neurons. These results do not support the theory that chronic alcohol consumption is neurotoxic to hippocampal pyramidal neurons in humans." (19)

In this paper the focus will also be on the (temporary) reduced ability to transfer information to the long-term memory because of Blood Alcohol Concentrations (BAC).

The brain

Ryback (11) speculated that alcohol might impair memory formation by disrupting activity in the hippocampus. This speculation was based on the observation that acute alcohol exposure (in humans) produces a syndrome of memory impairments similar in many ways to the impairments produced by hippocampal damage. Specifically, both acute alcohol exposure and hippocampal damage impair the ability to form new long-term, explicit memories but do not affect short-term memory storage or, in general, the recall of information from long-term storage. One way the hippocampus is affected by alcohol is by one of its "service suppliers", the medial septum. The medial septum sends rhythmic excitatory and inhibitory signals to the hippocampus, causing rhythmic changes in the activity of hippocampal pyramidal cells. The theta rhythm is thought to act as a clock (not unlike RAM in your computer that also needs a refresh clock), increasing or decreasing the likelihood that information entering the hippocampus from cortical structures will be processed .

Manipulations that disrupt the theta rhythm also disrupt the ability to perform tasks that depend on the hippocampus (14). Alcohol disrupts the theta rhythm in large part by suppressing the output of signals from medial septal neurons to the hippocampus (14). Given the powerful influence that the medial septum has on information processing in the hippocampus, the impact of alcohol on cellular activity in the medial septum is likely to play an important role in the effects of alcohol on memory.

The neurons and neuron transmitters

A selectively alters the activity of specific complexes of proteins embedded in the membranes of cells (i.e., receptors) that bind neurotransmitters such as gamma–aminobutyric acid (GABA), **glutamate**, serotonin, acetylcholine, and glycine (9). In some cases, only a few amino acids appear to distinguish receptors that are sensitive to alcohol from those that are not (10). "It remains unclear exactly how alcohol interacts with receptors to alter their activity" (5).

Glutamate is an excitatory neurotransmitter involved in learning and memory (16, 17). The references 16, 17 also link glutamate to schizophrenia. Having made this link, a short investigation was conducted to investigate if there is a link between alcohol and schizophrenia through Glutamate. (Trust me I did not do a practical test on a subject, I just did some literature research). And I found "Glutamate Receptor Abnormalities in Schizophrenia: Implications for Innovative Treatments" a paper indeed implying a correlation between schizophrenia and Alcohol and a potential treatment that affect Glutamate (18).

Alcohol disrupts the ability to establish long-lasting heightened responsiveness to signal from other cells (12). This heightened responsiveness is also known as long-term potential (LTP).

To establish LTP in the hippocampus it is required that a signal receptor (2 N–methyl–D–aspartate) NMDA becomes activated. NMDA is a receptor for neurotransmitter glutamate.

Alcohol interferes with the activation of NMDA receptor. (13)

Conclusions

Alcohol primarily affects the ability to form new long-term memories. It does not affect existing long-term memories nor on the ability to keep new information active in the short-term memory for a few seconds or more. The effect of alcohol on the transfer to long-term memories is also dependent on other factors like the speed of increase of the concentration of alcohol in the blood.

The effect of alcohol on the brain is manifold, but the effect on the memory is primary through two mechanism. At first it affects the neurotransmitters directly; secondly it affects the "clock" of the hippocampus, the medial septum.

By correlating the effect on the hippocampus of alcohol, with factual brain damage on patients in the same region it is clear that the hippocampus is crucial in the storage of long-term memory.

Human cognitive neuropsychology learns us, by studying case where nature has gone wrong, how the human minds works. By studying different types of brain damage and correlating certain brain damage to certain (lack of) traits we can make a rudimentary map of which parts are involved in which functionality (21). This insights can then be used again to improve the therapies for these brain injured patients. Dissociations and Associations between patients with brain different brain injuries and (lack of) traits is primarily used to create the model of how our brain works. In this paper the effect on alcohol on the brain is studied compared to a model generated by studying the different brain injuries, to understand the effect of certain drugs on our brain.

References

1. Edith V. Sullivan, Ph.D.; R. Adron Harris, Ph.D.; and Adolf Pfefferbaum, M.D, "Alcohol's Effects on Brain and Behavior", 2010, online consulted on 09/03/2018 https://pubs.niaaa.nih.gov/publications/arh40/127-143.pdf
2. Atkinson @ Hildegar's Introduction to psychology 16th edition *Nolen-Hoeksma a.o. page 261
3. Atkinson @ Hildegar's Introduction to psychology 16th edition *Nolen-Hoeksma a.o.
4. Girardi, Judith S., (2002) 'Lorine Niedecker: Poetry in the Classroom' [online article]. Available: http://grad.cgu.edu/~girardij/webpage/lorineclassroom.html. (4 December 2002)
5. White, Aaron M. "What Happened? Alcohol, Memory Blackouts, and the Brain." National Institute on Alcohol Abuse and Alcoholism, U.S. Department of Health and Human Services, July 2004, pubs.niaaa.nih.gov/publications/arh27-2/186-196.htm
6. [online] https://psychologyrats.edublogs.org/files/2012/02/Unit_3_2012_INSJ_Models-of-memory-23g15dl.pdf retrieved 10/03/2018
7. CRAIK, F.I.M., and LOCKHART, R.S. Levels of processing: A framework for memory research. Journal of Verbal Learning and Verbal Behavior 11:671–684, 1972.

8. Atkinson @ Hildegar's Introduction to psychology 16th edition *Nolen-Hoeksma a.o. page 246
9. LITTLE, H.J. The contribution of electrophysiology to knowledge of the acute and chronic effects of ethanol. Pharmacology and Therapeutics 84:333–353, 1999.
10. PEOPLES, R.W., and STEWART, R.R. Alcohols inhibit N–methyl–D–aspartate receptors via a site exposed to the extracellular environment. Neuropharmacology 10:1681–1691, 2000.
11. RYBACK, R.S. Alcohol amnesia: Observations in seven drinking inpatient alcoholics. Quarterly Journal of Studies on Alcohol 31:616–632, 1970.
12. BLISS, T.V.P., and COLLINGRIDGE, G.L. A synaptic model of memory: Long-term potentiation in the hippocampus. Nature 361:31–39, 1993.
13. SCHUMMERS, J., and BROWNING, M.D. Evidence for a role for GABA(A) and NMDA receptors in ethanol inhibition of long-term potentiation. Brain Research 94:9–14, 2001.
14. GIVENS, B.; WILLIAMS, J.M.; and GILL, T.M. Septohippocampal pathway as a site for the memory–impairing effects of ethanol. Hippocampus 10:111–121, 2000.
15. Alison R. Preston, Howard Eichenbaum, "Interplay of hippocampus and prefrontal cortex in memory" online https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3789138/pdf/nihms516381.pdf retrieved 11/03/2018
16. Atkinson @ Hildegar's Introduction to psychology 16th edition *Nolen-Hoeksma a.o. page 42
17. Geilenkotten Kristof, "mindmap from course notes" online http://geilenkotten.homeunix.org/~gws/images/Psychology8.jpg
18. María D. Rubio, Jana B. Drummond and James H. Meador-Woodruff , "Glutamate Receptor Abnormalities in Schizophrenia: Implications for Innovative Treatments" online https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3792192/pdf/ooomb4-20-1.pdf retrieved 11/03/2018
19. A.J. Harding, A. Wong, M. Svoboda, J.J. Kril, G.M. Halliday, "Chronic alcohol consumption does not cause hippocampal neuron loss in humans" Journal Hippocampus 1997 online http://onlinelibrary.wiley.com/doi/10.1002/(SICI)1098-1063(1997)7:1%3C78::AID-HIPO8%3E3.0.CO;2-3/full
20. Craik, K. (1943). The nature of explanation, Cambridge: Cambridge University Press
21. Ellis, A. W. and Young, A. W., (1996). Human Cognitive Neuropsychology: A Textbook with Readings. Philadelphia,Psychology Press.