The ascending arousal system and its impact on cognition

Lloyd, B.

Summary

Arousal plays a crucial role in how our brain functions, influencing thoughts, emotions, and behaviour. Some people naturally experience higher or lower levels of arousal, which can shape their personality and even impact mental health. However, arousal is not static; it fluctuates throughout the day. For example, if you're studying in a quiet room and suddenly hear a loud noise, your arousal level will increase, making you more alert but potentially also distracting you. Research shows that too little arousal can leave us sluggish and unfocused, while too much can make us feel stressed and overwhelmed. This relationship is described by the "Yerkes-Dodson Law", which is often illustrated as an upside-down U: moderate arousal leads to optimal performance, while extremes on either end can be detrimental.

Understanding brain arousal is essential, as arousal regulates daily activities, governs sleep patterns, and shapes the body's response to stress—all of which are crucial for overall health and well-being. Arousal is controlled by several chemical systems in the brain, including those involving noradrenaline, dopamine, serotonin, and acetylcholine. These chemicals help regulate alertness and readiness to respond. They work together in a larger system known as the *ascending arousal system*. The ascending arousal system is made up of several small brain regions situated deep in the middle of the brain. While we are still learning how these individual systems interact, tools like brain imaging and pupil size measurements are helping to uncover their role in arousal and behaviour.

This thesis contributes to a deeper understanding of the arousal system and holds potential for improving treatments for arousal-related disorders. It also advances knowledge of key brain areas implicated in neurological conditions like Alzheimer's and Parkinson's disease. The research in this thesis explored the ascending arousal system from three distinct angles: by examining natural fluctuations in arousal, using a non-invasive brain stimulation device to modulate arousal levels, and investigating how variations in arousal levels influence cognition, with a particular focus on memory formation.

In the first part, we aimed to measure natural arousal fluctuations. **Chapter 2** focuses on how arousal levels change on their own when people are at rest. By measuring pupil size and brain activity at the same time, we found that changes in pupil size reflect activity in arousal-related brain areas. The results from this study challenge the long-held idea that pupil size (which is understood to reflect changes

in arousal levels) is only driven by the locus coeruleus (a structure that mainly releases noradrenaline into the brain), but is also linked to the wider arousal system, including brain regions which release dopamine, serotonin and acetylcholine throughout the brain.

In the second part, this thesis examines whether a technique called *transcutaneous vagus nerve stimulation* (tVNS) can alter arousal levels. tVNS is a small handheld device which aims to deliver mild electrical stimulation to the vagus nerve, through placing electrodes on the skin of the ear. However, since this device is quite new, more research is needed to validate whether it effectively stimulates the proposed regions of the brain. **Chapter 3** found that tVNS caused pupils to dilate (a sign of increased arousal) but did not affect brain waves as expected. **Chapter 4** tested whether tVNS could increase motivation for rewards, but the results did not confirm this. These findings suggest that more research is needed to understand how tVNS affects arousal and behaviour.

The final section (**Chapters 5–7**) explores the relationship between arousal and memory. Several studies investigated whether anticipating a reward enhances memory formation. Specifically, we aimed to elevate arousal levels by pairing a stimulus image with the potential to receive a reward. This moment of reward anticipation led to measurable changes in brain activity, pupil size, and behaviour, all indicating heightened arousal.

We then examined whether these arousal-induced changes improved memory for the stimuli. Results showed that participants remembered reward-related items better. Smaller pupil responses—suggesting moderate arousal—were associated with better memory, while no direct link was found between brain activity in the ascending arousal system and memory. Another experiment revealed that arousal influenced memory accuracy (remembering having seen an object or not) but did not enhance the precision of recalled details (remembering exactly where that object was in space).

In summary, the arousal system is complex, involving multiple brain chemicals and regions that affect cognition in different ways. This research took a broad approach to understanding how changes in arousal can be captured through brain activity, pupil size and behaviour. We showed that simple, non-invasive measures like tracking pupil size can reliably reflect activity in the ascending arousal system and help assess the effects of brain stimulation and arousal-related changes. However, our findings also reveal that not all methods of influencing arousal work as expected, emphasising the need for a better understanding of how to target this system effectively. As research advances and technology improves, it will be possible to gain deeper insights into the ascending arousal system, which could lead to more effective studies and even new treatments in the future.