

RECENT HIGH-IMPACT PAPERS FROM RADBOUDUMC RESEARCHERS

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With over 3000 publications per year, scientific research is a cornerstone of the Radboud University Medical Centre (Radboudumc). In this section, recent high-impact papers – published by researchers from the Radboudumc – will be discussed.

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The road to superior memory

According to researchers from the Donders Institute and collaborators, superior memory can be trained using so-called mnemonic strategies. Twenty-three memory athletes from the top 50 of the memory sports world ranking list, known to be trained in mnemonic strategies, were examined. Functional magnetic resonance imaging (fMRI) was used to evaluate brain anatomy and function during rest and during participation in a word learning task. Compared to participants in the control group, these athletes demonstrated the capacity to correctly recall significantly more words shortly after encoding. Next, untrained controls were assigned to six weeks of mnemonic training, which significantly improved memory performance compared to active controls undergoing a different type of training (n-back working memory training) and passive controls without training. The effect persisted for at least four months. Additionally, fMRI analyses revealed that changes in brain connectivity induced by mnemonic training were correlated with the network organization underlying mnemonic expertise. Moreover, a superior memory capacity can be attributed to changes in functional connectivity, rather than adaptations in single brain regions. Results from this study could inspire the implementation of novel strategies to improve memory [1].

Reward-processing in addictive behaviour

People with addictive behaviour, such as substance users and gamblers, show disrupted reward processing, known as the reward deficiency syndrome theory. Researchers from the Radboudumc and collaborators characterized these disruptions more accurately during both anticipation and outcome notification of (non-addiction related) monetary rewards. In an image-based meta-analysis, fMRI of individuals with addictive behaviour (substance and gambling) showed decreased striatal activation during reward anticipation compared to healthy controls. The striatum is a critical brain region in the reward system: a decreased activity indicates low expectancy of the reward, which is in line with the reward-deficiency theory. During reward outcome, however, individuals with substance addiction show hyperactivity in the ventral striatum, which can be explained by the learning-deficit theory. As rewards are critical in learning processes, the authors suggest that the individuals fail to predict upcoming rewards, reflecting a learning deficit. During (unexpected) reward outcome, this results in abnormally large errors, accompanied by enhanced ventral striatum activity. Uncovering the mechanisms contributing to addiction could further guide the development of adequate treatment [2].

Neurons on a chip - visualized

Using neurons derived from human induced Pluripotent Stem Cells (hiPSCs), researchers from the Radboudumc and Radboud University developed a protocol to study neuronal networks on a chip. By forced expression of the transcription factor neurogenin-2, as previously described [3], a homogeneous population of excitatory neurons could be created in a rapid and efficient manner. Next, microelectrode arrays, with electrodes embedded in a substrate on which the cells can be cultured, were used to measure and characterize the electrophysiological properties of the neuronal networks. This method will allow the comparison of different (e.g. patient-specific) hiPSC lines as well as provide robust consistency for pharmacological studies. Remarkable about this study is that the results are published in the Journal of Visualized Experiments, which means that the entire protocol can be watched online [4].

References

1. Dresler, M., et al. "Mnemonic Training Reshapes Brain Networks to Support Superior Memory." *Neuron*. 93.5 (2017): 1227-35.e6. doi: 10.016/j.neuron.2017.02.003.
2. Luijten, M., et al. "Disruption of Reward Processing in Addiction : An Image-Based Meta-Analysis of Functional Magnetic Resonance Imaging Studies." *JAMA Psychiatry* 1.10 (2017). Radboudumc. "Radboudumc Jaardocument 2015"
3. Zhang, Yingsha, et al. "Rapid Single-Step Induction of Functional Neurons from Human Pluripotent Stem Cells." *Neuron* 78.5 (2013): 785-98.
4. Frega, Monica, et al. "Rapid Neuronal Differentiation of Induced Pluripotent Stem Cells for Measuring Network Activity on Micro-Electrode Arrays." *Journal of visualized experiments : JoVE*. 119 (2017).