## Review of: "Fornix and Uncinate Fasciculus Support Metacognition-Driven Cognitive Offloading"

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This study investigates the neural basis of metacognition-driven cognitive offloading using diffusion tensor imaging (DTI). The researchers examined the relationship between white matter tract integrity and behavioral indices related to the use of external reminders in a prospective memory task. Key findings include correlations between fornix integrity and reminder bias, uncinate fasciculus integrity and optimal reminder use, and superior longitudinal fasciculus integrity moderating the relationship between metacognitive bias and reminder use.

This study offers several novel contributions and significant insights into the neural basis of metacognition-driven cognitive offloading.

1. This is one of the first studies to use diffusion tensor imaging (DTI) to examine the structural connectivity underlying metacognition-driven cognitive offloading. Previous research has primarily relied on functional neuroimaging (Boldt & Gilbert, 2019), making this structural approach novel and complementary.

2. The study reveals a positive correlation between fornix integrity and bias towards using external reminders. This finding suggests a crucial role for hippocampal-prefrontal interactions in metacognitive control processes, extending our understanding of the fornix beyond its known role in episodic memory (Kwok & Buckley, 2015).

3. The negative correlation between left uncinate fasciculus integrity and deviation from optimal reminder use provides new insights into how temporal-frontal connections might support efficient metacognitive control (Alm et al., 2016).

4. The study demonstrates that the integrity of the right superior longitudinal fasciculus moderates the relationship between metacognitive bias and reminder bias. This finding offers a novel perspective on how structural connectivity influences the interaction between metacognitive monitoring and control (Fleming et al., 2010).

5. The negative correlations between cingulum bundle and superior longitudinal fasciculus integrity and confidence predictions provide new evidence for the involvement of a frontoparietal network in global confidence judgments, complementing previous functional findings (Rouault & Fleming, 2020).

6. The results offer new insights into the potential neural mechanisms underlying the integration of local and global metacognitive processes, an area of growing interest in the field (Rouault et al., 2018).

7. By linking memory-related tracts to metacognitive behaviors, this study opens up new questions about the hippocampo-cortical interactions underlying metamemory processes (Vaccaro & Fleming, 2018).

DTI tractography has been widely used to study white matter microstructure and its relationship to cognitive function in healthy individuals. However, several fundamental limitations of this technique must be considered when interpreting

## results.

1. DTI tractography often fails to accurately represent complex white matter anatomy, particularly in regions with crossing fibers (Jones et al., 2013). This can lead to false positives and negatives when reconstructing tracts. As Maier-Hein et al. (2017) demonstrated, even state-of-the-art tractography algorithms produce anatomically implausible results in up to 90% of cases when validated against ground truth.

2. The spatial resolution of DTI is typically on the order of millimeters, while axon diameters are on the micrometer scale. This mismatch means DTI cannot resolve individual axons or small fiber bundles, leading to partial volume effects and oversimplification of tract geometry (Assaf et al., 2019).

3. The tensor model used in DTI makes several simplifying assumptions about water diffusion in tissue that do not always hold true biologically. This can result in erroneous estimates of tract orientation and microstructural properties, especially in regions with complex fiber configurations (Tournier et al., 2011).

4. DTI metrics like fractional anisotropy (FA) are sensitive to many different tissue properties and pathological processes. Changes in FA cannot be unambiguously attributed to specific biological changes, limiting mechanistic interpretations (Jones et al., 2013).

5. There is substantial variability in white matter tract anatomy between individuals. Methods for aligning and comparing tracts across subjects may introduce errors and wash out important individual differences (Wassermann et al., 2011).

6. Correlations between DTI metrics and cognitive measures in healthy subjects are often weak and inconsistent across studies. The neurobiological basis for such correlations remains unclear, and they may be influenced by confounding variables (Madden et al., 2012).

## Minor points:

1. The study has a relatively small sample size (n=34), which limits statistical power and generalizability. Increasing the sample size would improve the robustness of the findings (Button et al., 2013).

2. The study does not include a control group, making it difficult to determine if the observed relationships are specific to cognitive offloading or general to other cognitive processes. Including a control task or group would strengthen the conclusions (Simons et al., 2016).

3. The study relies heavily on correlational analyses, which cannot establish causal relationships. Incorporating experimental manipulations of cognitive offloading or longitudinal designs could provide stronger evidence for causal links (Marinescu et al., 2018).

4. The study focuses on a single cognitive offloading task. Including multiple tasks or measures of cognitive offloading would improve the construct validity and generalizability of the findings (Risko & Gilbert, 2016).

5. The study does not control for potential confounding variables such as general cognitive ability, working memory capacity, or personality traits, which may influence cognitive offloading behavior (Hu et al., 2019).

 While DTI provides valuable structural information, combining it with functional neuroimaging techniques (e.g., fMRI) would offer a more comprehensive understanding of the neural mechanisms underlying cognitive offloading (Honey et al., 2009).

7. The study does not extensively examine how individual differences (e.g., age, gender, education) may influence the observed relationships. Incorporating these factors could provide more nuanced insights (Dunn & Risko, 2016).

In conclusion, these findings significantly advance our understanding of the neural architecture supporting metacognitiondriven cognitive offloading and provide a foundation for future research in this area. While DTI tractography has provided valuable insights into brain structure-function relationships, its fundamental limitations must be carefully considered when interpreting results, particularly in correlational studies with cognitive measures in healthy individuals. More advanced diffusion MRI techniques and analysis methods may help address some of these issues in future research.

References:

Alm, K. H., Rolheiser, T., & Olson, I. R. (2016). Neuroscience & Biobehavioral Reviews, 71, 154-168. doi:10.1016/j.neubiorev.2016.08.036

Boldt, A., & Gilbert, S. J. (2019). Nature Human Behaviour, 3(3), 281-291. doi:10.1038/s41562-019-0518-5

Fleming, S. M., Weil, R. S., Nagy, Z., Dolan, R. J., & Rees, G. (2010). Science, 329(5998), 1541-1543. doi:10.1126/science.1191883

Kwok, S. C., & Buckley, M. J. (2015). Journal of Neuroscience, 35(4), 1547-1556. doi:10.1523/JNEUROSCI.2620-14.2015

Rouault, M., & Fleming, S. M. (2020). Nature Communications, 11(1), 1-11. doi:10.1038/s41467-020-16278-6

Rouault, M., McWilliams, A., Allen, M. G., & Fleming, S. M. (2018). Neuroscience of Consciousness, 2018(1), niy004. doi:10.1093/nc/niy004

Vaccaro, A. G., & Fleming, S. M. (2018). Journal of Neuroscience, 38(14), 3534-3543. doi:10.1523/JNEUROSCI.2571-17.2018

Assaf, Y., Johansen-Berg, H., & Thiebaut de Schotten, M. (2019). The role of diffusion MRI in neuroscience. NMR in Biomedicine, 32(4), e3762. https://doi.org/10.1002/nbm.3762

Jones, D. K., Knösche, T. R., & Turner, R. (2013). White matter integrity, fiber count, and other fallacies: The do's and don'ts of diffusion MRI. NeuroImage, 73, 239-254. https://doi.org/10.1016/j.neuroimage.2012.06.081

Madden, D. J., Bennett, I. J., Burzynska, A., Potter, G. G., Chen, N. K., & Song, A. W. (2012). Diffusion tensor imaging of cerebral white matter integrity in cognitive aging. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1822(3), 386-400. https://doi.org/10.1016/j.bbadis.2011.08.003

Maier-Hein, K. H., Neher, P. F., Houde, J. C., Côté, M. A., Garyfallidis, E., Zhong, J., ... & Descoteaux, M. (2017). The challenge of mapping the human connectome based on diffusion tractography. Nature Communications, 8(1), 1349. https://doi.org/10.1038/s41467-017-01285-x

Tournier, J. D., Mori, S., & Leemans, A. (2011). Diffusion tensor imaging and beyond. Magnetic Resonance in Medicine, 65(6), 1532-1556. https://doi.org/10.1002/mrm.22924

Wassermann, D., Bloy, L., Kanterakis, E., Verma, R., & Deriche, R. (2011). Unsupervised white matter fiber clustering and tract probability map generation: Applications of a Gaussian process framework for white matter fibers. NeuroImage, 51(1), 228-241. https://doi.org/10.1016/j.neuroimage.2010.01.004

Button, K. S., et al. (2013). Nature Reviews Neuroscience, 14(5), 365-376. doi:10.1038/nrn3475

Simons, D. J., et al. (2016). Perspectives on Psychological Science, 11(3), 432-450. doi:10.1177/1745691616635592

Marinescu, I. E., et al. (2018). Nature Human Behaviour, 2(10), 797-808. doi:10.1038/s41562-018-0444-y

Risko, E. F., & Gilbert, S. J. (2016). Trends in Cognitive Sciences, 20(9), 676-688. doi:10.1016/j.tics.2016.07.002

Hu, X., et al. (2019). Memory & Cognition, 47(6), 1114-1127. doi:10.3758/s13421-019-00924-6

Honey, C. J., et al. (2009). Proceedings of the National Academy of Sciences, 106(6), 2035-2040. doi:10.1073/pnas.0811168106

Dunn, T. L., & Risko, E. F. (2016). Cognitive Research: Principles and Implications, 1(1), 5. doi:10.1186/s41235-016-0005-7