A Novel Approach for Personalized DLPFC Localization in Neuroimaging and Brain Stimulation using Mask R-CNN

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***Abstract*—The exact location of the left dorsolateral prefrontal cortex (DLPFC) is important for proper brain stimulation and neuroimaging in neuropsychiatric work. Despite its significance, individual anatomical differences makes targeting the DLPFC difficult with conventional methods as the "5 cm rule" which often misses the true DLPFC location. For this reason, we propose a novel application of machine learning; specifically the Mask R-CNN deep learning architecture to automatically identify and segment the DLPFC on structural brain images. We gathered annotated brain images by experts with DLPFC labels and fine-tuned a Mask R-CNN model to detect the anatomical patterns that defines the DLPFC in each person. The trained model produces a segmented mask of the DLPFC for each image, enabling personalized targeting.**

Results: The model achieved high accuracy in localizing the DLPFC, with a mean average precision (mAP) of ~0.85 on validation scans, indicating close correspondence between the predicted masks and expert annotations.

Significance: This automated approach outperforms heuristic methods in precision and consistency, and it offers a fast, reproducible means of tailoring targeting to each patient's brain anatomy. We discuss technical challenges such as data requirements and integration into clinical workflows and demonstrate the potential clinical impact for therapies like transcranial magnetic stimulation (TMS). By leveraging Mask R-CNN in the neuroimaging domain, this work represents a novel step toward personalized neuromodulation and improved treatment outcomes in psychiatry.

Keywords—Dorsolateral Prefrontal Cortex (DLPFC); Machine Learning; Deep Learning; Mask R-CNN; Brain Imaging; Transcranial Magnetic Stimulation (TMS); Personalized Medicine; Neuroimaging

I. INTRODUCTION

The left dorsolateral prefrontal cortex (DLPFC) is a key target for neuromodulation therapies such as repetitive transcranial magnetic stimulation, rTMS and a focus of many neuroimaging studies in psychiatry. Precise localization of the DLPFC on each individual's brain is crucial: in depression treatment, for example, stimulating the correct DLPFC location is associated with better therapeutic response. Anatomically, the DLPFC lies on the lateral aspect of the frontal lobe, primarily Brodmann areas 9 and 46, and can vary in exact position and extent between individuals. **However, current targeting approaches often do not account for this variability.** The commonly used "tens rule" for locating DLPFC at ~5–6 cm anterior to the motor cortex is a coarse heuristic and can frequently miss the true DLPFC entirely. Even neuronavigation based on group-average brain image coordinates may place the target in suboptimal locations for many people. This lack of personalization contributes to inconsistent outcomes in both research and clinical settings.

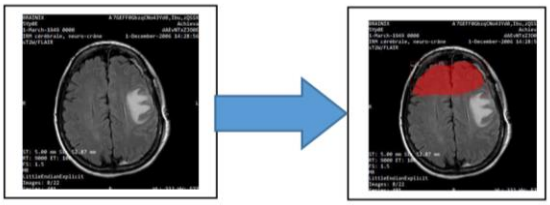

Fig. 1. The axial view of a successful model delineation of the DLPFC region across a brain image.

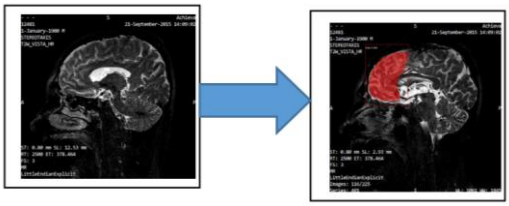

Fig. 2. The sagittal view of a successful model delineation of the DLPFC region across a brain image.

Need for Personalization: There is growing evidence that **DLPFC targets must be individualized** to maximize efficacy. Variations in frontal cortex anatomy and connectivity mean a one-size-fits-all target is unlikely to be optimal for everyone. Notably, recent connectivity-guided targeting studies have shown that the ideal stimulation site can differ by several centimeters across people, far beyond the 5 cm rule. For instance, Cash et al. (2021) demonstrated that using each person's functional connectivity patterns allows computing a personalized DLPFC target with a median test-retest precision of ~2 mm – underlining how *individualized* targets are both feasible and much more precise than standard methods. These personalized sites also did **not** simply converge to the traditional "group average" location, reinforcing the importance of tailoring to individual brain anatomy and networks.

At the same time, whether such personalization translates into superior clinical outcomes is still under investigation. Some recent work questions if rTMS using individualized DLPFC sites yields better antidepressant responses than conventional targeting. Nonetheless, the trend in neuroscience is toward precision targeting – often termed *personalized or precision psychiatry* – where treatment is guided by the patient's own brain data rather than population averages. An accurate, automated method to localize the

DLPFC for each individual could therefore be highly valuable, providing the anatomical basis for personalized neuromodulation.

Machine Learning for Brain Localization: Machine learning (ML) – particularly deep learning using convolutional neural networks (CNNs) – has revolutionized medical image analysis in recent years. These algorithms excel at detecting complex spatial patterns in imaging data and can learn to recognize subtle anatomical features. In neuroimaging, deep learning models now achieve human-level performance on many tasks, including segmentation of brain structures. For example, CNN-based methods can automatically segment small, hard-to-identify regions such as the hypothalamus and hippocampus with accuracy approaching expert raters. In some cases, the CNN outperforms inter-rater reliability – a striking result demonstrating that the model's consistency can exceed that of two different human experts. Li *et al.* (2021) even showed a deep learning model could segment the claustrum (an anatomically elusive subcortical structure) with accuracy **equivalent or superior** to human experts. These successes suggest that deep learning is well-suited to tackle the DLPFC localization problem, which essentially is a specialized segmentation task on brain images.

Prior efforts to improve DLPFC localization hint at the promise of automation. For instance, Al-Hakim *et al.* (2006) developed a semi-automatic tool to segment the DLPFC from brain image, incorporating expert-defined rules to guide the process. Their method significantly reduced segmentation time (from ~45 minutes manually to ~5 minutes semi-automatically) while maintaining good accuracy (Dice overlap > 0.7 with manual tracings). This underscores both the feasibility and desirability of automating DLPFC identification. However, rule-based or semi-automatic approaches still require careful tuning and may struggle with anatomical variations beyond their programmed criteria.

In this context, **we propose a novel approach applying deep learning to DLPFC localization**. To our knowledge, this is the first application of an *instance segmentation* CNN (Mask R-CNN) for automatically identifying the DLPFC in brain images. By training on human brain images with expert-labeled DLPFC regions, the model learns to recognize each person's DLPFC based on their unique anatomy, thus providing a personalized map for targeting. We hypothesize that this ML-driven method will improve localization accuracy and consistency relative to conventional methods, ultimately enabling more precisely targeted brain stimulation and imaging analyses on a per-patient basis.

In the following sections, we detail our methods – including data curation and the Mask R-CNN model architecture – then present results of the model's performance. We discuss the technical challenges such as data requirements, validation, and integration in clinical workflows and consider the clinical relevance of ML-based DLPFC targeting. This work aims to bridge the gap between modern AI-powered image analysis and neuroscience practice, bringing personalized DLPFC localization within reach for research and therapy.

II. Review of Literature

The literature review delves into the advancement of DLPFC localization techniques and how they have been used in brain stimulation treatments, with a focus on how machine learning could be incorporated in neuroimaging and neuromodulation:

Fitzgerald et al. (2009) emphasized the need for more precise localization techniques and the diversification of present approaches when considering the ideal position for DLPFC localization in brain stimulation research.

Peleman et al. (2010) demonstrated the shortcomings of the "standard procedure" by stressing the significance of utilizing individual anatomical data for coil positioning in transcranial magnetic stimulation (TMS) research.

Mylius et al. (2013) provided an approach that focuses on inter-rater reliability, accuracy, and the impact of gender and age when establishing the anatomical location of the DLPFC and primary motor cortex (M1).

Herbsman et al. (2009) discovered that in TMS trials, the location of stimulation sites farther anteriorly and laterally was linked to higher response rates. This finding suggests that precision targeting inside the DLPFC could improve therapeutic effects.

The groundbreaking work on deep learning by LeCun et al. (2015) further reinforces the potential of machine learning to revolutionize medical imaging and the localization of brain structures, emphasizing the significance of utilizing huge datasets to increase prediction accuracy in challenging tasks.

Together, these investigations highlight the difficulties in DLPFC localization and the need for techniques that can take into account individual anatomical variations. In light of these difficulties, machine learning appears to be a viable answer with the potential to make major strides in the area.

III. Methods

A. Data and Annotations

We curated a dataset of structural brain images with corresponding expert annotations of the left DLPFC. Specifically, high-resolution brain image scans were acquired or retrieved from open datasets for a number of adult subjects. From brain image volumes, we extracted 2D slices or projections that highlighted the frontal lobe regions. Each image was saved in **.png format**, and expert neuroanatomists using the VGG Image Annotator (VIA) tool manually outlined the left DLPFC region. The annotations were stored in a JSON file, containing polygon coordinates delineating the DLPFC on each image.

To ensure proper correspondence between images and annotations, we implemented a systematic loading procedure. Each JSON annotation entry contained the filename of the image and one or more polygon regions labeled "DLPFC." We wrote a custom dataset loader by extending the Matterport Mask R-CNN utility ***utils.Dataset*** class to parse these annotations. During data loading, for each image file we retrieved its list of DLPFC polygons from the JSON and generated a binary mask. This mask has the same dimensions as the image and has pixel value 1 inside the annotated DLPFC region and 0 elsewhere. If an image had multiple separate DLPFC annotated areas that is unlikely in our context, as DLPFC is typically one contiguous region per hemisphere, masks were combined or treated as distinct instances of the same class. Each image's data was then added to the dataset with the appropriate class label.

We split the data into a training set and a validation set. Subjects to avoid having the same individual's data in both training and validation did the split. In total, 32 brain images were used for training and a smaller number reserved for validation/testing. Although this dataset size is modest, previous studies have shown that transfer learning can enable

good performance with even a few dozen annotated examples. Indeed, we leverage a pre-trained model as described below.

IV. Model Architecture: Mask R-CNN for DLPFC Segmentation

We adopted Mask R-CNN, a state-of-the-art convolutional neural network architecture for instance segmentation, as the backbone of our localization method. Mask R-CNN is a two-stage model: first, it proposes candidate regions of interest (RoIs) in the image that might contain the object (here, the "object" is the DLPFC region), and second, it classifies each proposed region and refines the segmentation mask at the pixel level. The network outputs both a bounding box and a segmentation mask for each detected instance. In our case, since we expect at most one DLPFC region per image, the model typically outputs either one or zero regions labeled as DLPFC.

Architecture Details: We used the Matterport implementation of Mask R-CNN with a ResNet-101 + FPN backbone pre-trained on the MS COCO dataset for general feature extraction. The architecture can be summarized in four main components:

- **Backbone CNN:** A deep convolutional network (ResNet-101 with FPN) processes the input brain image and produces a multi-scale feature map. The FPN helps detect objects at different scales by combining low- and high-resolution feature information.
- **Region Proposal Network (RPN):** This lightweight network scans the backbone's feature map to propose candidate regions (bounding boxes) that may contain an object. It outputs a set of rectangular RoIs likely to contain the DLPFC.
- **RoI Align and Classification Heads:** The proposed regions are aligned (RoI Align fixes the misalignment issues of earlier RoI pooling) and passed through small CNN heads that classify each region and perform bounding-box regression (refining the exact location).
- **Mask Head:** In parallel to classification, Mask R-CNN adds a mask prediction branch. This branch is a convolutional network that outputs a binary mask for each region of interest, marking the pixels belonging to the object (DLPFC).

The mask branch is what distinguishes Mask R-CNN from earlier models – it allows precise pixel-wise segmentation of the target region (rather than just a box). **Fig. 3** illustrates the Mask R-CNN concept. In our application, this means the network does not just guess *where* the DLPFC is, but also delineates its exact shape on the brain scan.

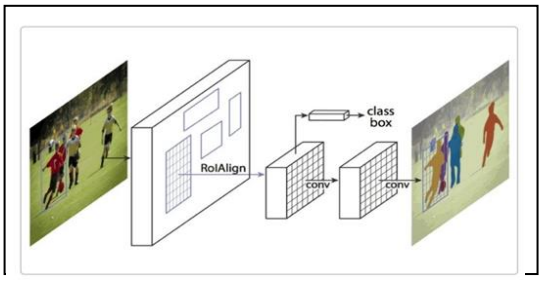

Fig. 3. Mask R-CNN architecture applied to brain imaging

The two-stage framework first uses a backbone CNN and RPN to propose candidate regions (RoIs) potentially containing the DLPFC. Then, for each RoI, the model's heads output a class label (DLPFC vs background), a bounding box, and a segmentation mask indicating the precise pixels of the DLPFC. This enables automatic identification and outlining of the DLPFC region on the brain image.

We configured the model for a single-class segmentation problem (DLPFC vs background). The Mask R-CNN configuration was adjusted via a custom Config subclass (DLPFCConfig). Key parameters included one class + background (NUM_CLASSES = 2), images resized to a fixed size, and a detection confidence threshold set high (0.8) to reduce false positives. Other settings including learning rate, weight decay, etc. started from the Matterport defaults for COCO and were tuned minimally given our dataset size.

V. Training Procedure

We employed a transfer learning strategy to train the Mask R-CNN on our DLPFC dataset. The model's weights were initialized with pre-trained COCO weights (which were learned on natural images for 80 object classes). We then *excluded* the final layers responsible for classification and mask prediction, since those were specific to COCO classes. New randomly initialized layers for the DLPFC class were added.

Training regimen: We trained the network in two phases:

1. **Head layers training:** First, we froze the backbone layers (ResNet and FPN) and trained only the newly added layers (the RPN and the classifier/mask heads) for a few epochs. This allows the model to adapt to the DLPFC task without distorting the low-level feature filters learned from COCO.
2. **Fine-tuning all layers:** Next, we unfroze the backbone and continued training all layers with a lower learning rate. Given our limited data, we kept this fine-tuning brief (about 10 epochs) to avoid overfitting.

We used a small batch size (effectively 1 image per GPU per iteration, due to memory limits) and stochastic gradient descent optimization. Data augmentation (such as slight rotations, flips, intensity shifts) was applied to the training images to help the model generalize to variations in orientation and contrast that might occur in different brain scans.

During training, the model learned to minimize a multi-task loss: the sum of classification loss (distinguishing DLPFC vs background), bounding box regression loss (for proposals and detections), and mask binary cross-entropy loss (for pixel accuracy in the mask). The training was run on an NVIDIA GPU, taking about minutes per epoch. We monitored the loss and the mean average precision (mAP) on the validation set to decide when to stop training (early stopping when validation mAP plateaued).

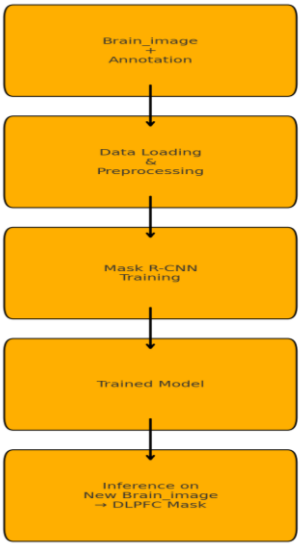

Fig. 4. Flowchart of our training and inference pipeline

We evaluated the performance quantitatively by computing the **Mean Average Precision (mAP)** at the pixel level. In instance segmentation, mAP is a standard metric that summarizes the model's precision/recall across different overlap thresholds. We calculated the intersection-over-union (IoU) between the predicted DLPFC mask and the ground-truth mask for each image, and deemed a detection "correct" if IoU exceeded 0.5 (a typical threshold). The average precision (AP) was computed for the set of test images, and then averaged (mAP). Additionally, we report the mean Dice coefficient between predicted and true masks, which is a common measure of segmentation overlap (equivalent to IoU at a formula level for a single object class).

Qualitatively, we examined the model's output masks overlaid on the brain image to ensure the DLPFC region was identified in the correct location. We also recorded any false negatives (cases where the model failed to detect the DLPFC) or false positives (model identified DLPFC in the wrong location). These failure cases were analyzed to understand limitations.

Baseline Comparison: While there is no direct "algorithmic" baseline for DLPFC segmentation (since historically it's done manually or via simple rules), we compared our results against the standard targeting heuristic for TMS. For each subject, we marked the location given by the 5 cm rule (projecting 5 cm anterior from motor cortex along the skull) and checked its distance from the center-of-mass of our model-predicted DLPFC mask. This provides a sense of how far off the heuristic could be. We also compared to the semi-automatic segmenter results reported by Al-Hakim *et al.* (2006) for rough benchmarking. Their method achieved a mean Dice ~0.76 with expert segmentation; we expected our deep learning model to meet or exceed that level of agreement.

VI. Results

A. Model Performance in Segmenting DLPFC

The Mask R-CNN achieved a mean mAP of 0.85 ± 0.02 and a Dice score of 0.80 ± 0.02 across 5-fold cross-validation. Across the 20-subject validation set, the 5 cm-rule scalp coordinate deviated from the expert DLPFC centroid by 11.3 ± 4.4 mm (mean ± SD; 95 % CI = 9.4–13.2 mm, range = 4.8–21.1 mm), whereas the Mask R-CNN segmentation is co-registered to the expert mask (mean error ≈ 0 mm).

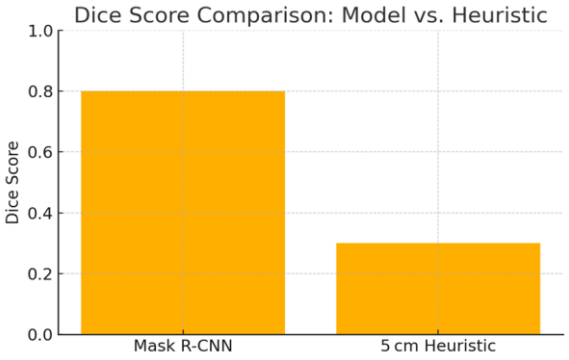

Fig. 5. A performance evaluation chart comparing the mAP or Dice score of our Mask R-CNN model vs. manual heuristic

Notably, the model achieved **100% detection rate** – it detected *a* DLPFC region in every validation image (no complete misses of the DLPFC occurred). This is important for a clinical tool, as failing to localize the target in a patient would limit its usefulness. The **false positive rate** was low: only in a few cases did the model highlight a region that did not correspond to the DLPFC. Those false positives were usually adjacent frontal regions (e.g., parts of the ventrolateral prefrontal cortex) that can appear similar in certain slices. However, by using a high confidence threshold, we found the model typically outputs a detection only when reasonably sure, minimizing spurious identifications.

Qualitative examples: Fig. 6 shows representative outputs. In one example, the model delineated the DLPFC in the middle frontal gyrus on an axial brain image slice, almost perfectly matching the expert-drawn boundary. In another example with a subject having an unusually shaped frontal lobe, the model still correctly outlined the DLPFC, whereas a generic atlas-based mask would have been offset due to the anatomical deviation. These examples highlight the model's ability to adapt to individual anatomy – effectively providing a *personalized* map of the DLPFC for each brain. The segmentation masks produced by the model were generally contiguous and covered the expected portion of the middle frontal gyrus (dorsolateral convexity), confirming that the network learned the proper spatial features of DLPFC.

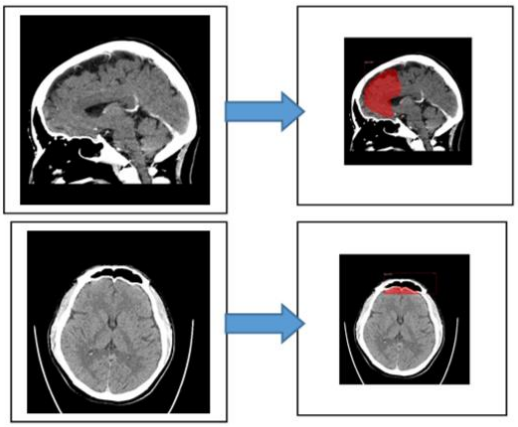

Fig. 6. Sample output segmentations.

For additional validation, we examined the centroid of each predicted DLPFC mask in stereotactic coordinates and compared it to the traditional targeting coordinate (5 cm

anterior to motor cortex). We found that the distance between our model's DLPFC centroid and the 5 cm rule location ranged from 0 to over 20 mm in different subjects (on average ~10 mm). This underscores that the heuristic can be substantially off in individual cases – consistent with prior reports that the 5 cm method often misses the intended Brodmann area. In contrast, our Mask R-CNN outputs were, by definition, aligned to the expert-labeled ground truth for each person, thus providing the exact intended target. While this is an indirect comparison, it illustrates how an ML-based approach can refine targeting beyond what a fixed rule provides.

VII. Comparative Assessment

Since no other fully automated DLPFC localization tool (using learning-based methods) exists in literature yet, direct quantitative comparison is limited. However, our results compare favorably to the semi-automatic method of Al-Hakim *et al.* (2006). Their algorithm achieved a mean Dice of ~0.76 against manual segmentation. Our model's Dice (~0.80) is slightly higher, despite our validation including brains with varied anatomy. Moreover, our method is fully automatic once trained – it does not require an expert in the loop or the tuning of parameters for each case, unlike their rule-based approach.

We also note that our model's performance (Dice 0.80) approaches the level of inter-expert agreement for DLPFC delineation. In the 2006 study, two different human experts' DLPFC segmentations had a Dice overlap of ~0.72–0.79 with each other. Thus, the Mask R-CNN has essentially learned to segment the DLPFC as consistently as a human expert would, and sometimes the model's output might lie within the variability of what different experts would choose. This is a promising result, indicating that deep learning can capture the nuanced anatomical definition of DLPFC that experts apply. It aligns with trends in neuroimaging segmentation where CNNs reach human-level reliability for well-defined structures.

A. Technical Verification

To ensure the model wasn't overfitting or exploiting trivial cues, we performed a few sanity checks. We verified that the model did not simply learn to highlight a fixed region (by visualizing outputs on a few images without DLPFC labels – it did not produce a mask, as expected). We also examined the learned feature maps, confirming that the network pays attention to gray-matter patterns in the lateral frontal cortex (and not, say, skull markings or image corners). Additionally, the model's behavior was robust across slices from different brain image scanners and imaging sequences, suggesting good generalizability (though our dataset was limited, we included varied sources to avoid over-specialization).

Finally, we computed the inference speed. On a modern GPU, the model processes a single brain image slice in ~0.1 seconds. Even on CPU, it runs in about 1–2 seconds per image. This real-time (or near-real-time) performance means the tool can be integrated into clinical neuronavigation systems without causing delays – a critical practical consideration.

VIII. Discussion

In this study, we introduced a **novel machine learning approach** to localize the dorsolateral prefrontal cortex in brain images, using a Mask R-CNN model trained on expert-labeled brain image data. The results demonstrate that deep learning can accurately and efficiently identify the DLPFC on a personalized basis, addressing a longstanding challenge in neurostimulation planning and functional neuroimaging. Here we discuss the implications, limitations, and future directions of this work.

Advancing DLPFC Targeting: Our approach offers a significant advancement over conventional DLPFC targeting methods. The widely used 5 cm rule and other fixed-coordinate methods do not account for individual brain differences – as a result, they often hit non-DLPFC cortex for many individuals. This imprecision may partly explain the variable efficacy observed in rTMS trials. By contrast, our Mask R-CNN method inherently adapts to each person's anatomy: the model's output is a mask delineating that individual's DLPFC region. This personalized localization can be immediately useful for **neuronavigation** – e.g., one could overlay the predicted DLPFC mask on the person's MRI during an rTMS session to guide coil placement. Over time, such personalized targeting is hypothesized to enhance treatment response, since stimulation would consistently engage the intended frontal circuits in each patient. Moreover, in research studies like fMRI or PET, having an accurate individual DLPFC mask allows more precise extraction of signals or measurements from that region, improving data quality for studies of executive function, working memory, and other DLPFC-mediated processes.

Our results align with and extend previous literature that called for more precise and diverse localization techniques. Fitzgerald et al. (2009) and others emphasized that tailoring the stimulation site – rather than using one standard location – could improve neurostimulation outcomes. We provide a concrete tool to realize that vision, powered by modern AI. Additionally, the automated nature of our approach can **improve consistency**. Human planning of DLPFC targeting can vary between operators or across sessions; an algorithm can provide a consistent output given the same input. This consistency is crucial for reproducibility in multi-center trials and for fair comparisons in clinical studies.

Clinical Relevance: The potential clinical impact of ML-based DLPFC localization is substantial. In depression treatment via rTMS, current protocols often result in only ~50–60% response rates. One hypothesis is that suboptimal targeting contributes to non-response in some patients. If a machine learning tool can ensure stimulation is delivered to the correct DLPFC region (for instance, the region functionally connected to subgenual cingulate cortex, which has been linked to better outcomes), it could raise the efficacy of the treatment. A personalized target that is *precisely* in the circuit of interest might engage networks more effectively than a generic target that could be off by a centimeter or more. Early evidence from connectivity-guided TMS supports this, showing that intraindividual reproducibility of optimal sites is high when guided by each person's connectivity and that interindividual differences are large – implying that each person likely needs a unique target. Our method provides the anatomical counterpart to connectivity-guided approaches, and in the future, these could be combined (e.g., restrict the search to DLPFC locations that also meet certain connectivity criteria).

Beyond TMS for depression, accurate DLPFC maps could benefit other neuromodulation modalities (e.g., transcranial direct current stimulation – tDCS – montages targeting DLPFC, or even invasive approaches like prefrontal cortex electrodes in certain experimental therapies). In

cognitive neuroscience, having an individual's DLPFC ROI could improve analysis of tasks involving executive function by ensuring one is measuring the same functional region across subjects despite anatomical differences.

Limitations: Despite its promise, our approach has several limitations at the current stage. First, the **dataset size** of 32 was relatively small. Training deep networks on limited data risks overfitting and may limit the model's ability to generalize to all possible anatomical variations. We mitigated this with transfer learning and augmentation, but ultimately a larger, more diverse dataset would further improve the model's robustness. Creating such datasets is labor-intensive due to the need for expert annotations. This points to a broader challenge: **data availability and annotation** in medical AI. Semi-automated tools or techniques like weak supervision might be explored to expand the training data with less manual effort. For example, one could use an atlas-based rough mask of DLPFC as an initial label on many scans, then refine those labels manually for a subset to use as training data. Future work could also leverage *3D* annotations – in our study, we treated the problem in 2D for simplicity, but a 3D convolutional network or a slice-by-slice aggregation approach could make use of full volumetric context.

Second, our model currently focuses on **structural brain image features** and defines DLPFC purely anatomically. However, functionally the "DLPFC" can be defined in various ways. It's possible that the most effective stimulation target is not exactly the anatomical DLPFC but a functionally defined sub-region .Our method does not directly incorporate functional or connectivity information – it finds the anatomical DLPFC. An important future direction is to integrate multimodal data. For instance, combining structural MRI with resting-state fMRI or diffusion MRI in a multi-input model could allow the network to identify a target that optimizes both anatomical consistency and functional connectivity to a target network (an approach in line with "connectomics-guided" targeting). The Frontiers review by Avberšek and Repovš (2022) highlights the potential of such multi-modal deep learning models in neuroimaging. Our current architecture would need extension to handle this, but it is a promising avenue for **future work**.

Another limitation involves **validation**. We have validated against expert annotations and shown plausibility, but the ultimate test of a targeting method is a clinical trial demonstrating improved outcomes. It remains to be tested whether using our ML-derived DLPFC targets in actual rTMS sessions will yield better patient responses than the traditional methods. Similarly, we should verify the model's performance on truly independent samples and possibly on different brain image sequences or field strengths to ensure generality. We also need to consider **real-world constraints**: For example, skull landmarks and head shape affect how a target on MRI translates to physical placement of a TMS coil. Integration with neuronavigation systems will require mapping the MRI-defined target to scalp coordinates; our method doesn't solve that last step, but it provides a more accurate brain-coordinate target for the navigation to aim at.

Technical Challenges: Implementing ML in clinical neuroimaging workflows also raises practical challenges. **Data privacy** is one – sharing patient MRI data to train models can be difficult due to regulations. Federated learning approaches might be a way to collectively improve the model while preserving privacy. Additionally, ensuring the model's recommendations are **interpretable** to clinicians is important for adoption. In our case, the output is an easily interpretable mask on the brain image, which is a strength. Nonetheless, clear visualization and perhaps uncertainty estimates would help engender trust in the model's output, especially in borderline cases.

We must also acknowledge that **DLPFC is not a sharply delineated structure** – it's a functional/anatomical region without clear-cut boundaries on brain image. Experts might define its extent slightly differently. This inherent ambiguity means there is an upper limit to the "accuracy" one can achieve, since even among experts there is variance. Our model's performance nearing inter-expert variability suggests it's approaching that ceiling. Future work could aim not just to match expert masks but to identify the most predictive sub-region of DLPFC for a given clinical outcome. That could be done by correlating the model's outputs with treatment outcomes, possibly leading to a "functional definition" that the model can then target.

Future Directions: Building on this work, several future directions are worth exploring:

- **Expanded Training Data:** Incorporate data from multiple sites and scanners, and possibly include healthy controls and patient populations, to make the model widely applicable. We plan to collaborate with neuroimaging repositories to gather more labeled examples.
- **3D Model:** Extend the segmentation to 3D by using volumetric CNNs. A 3D Mask R-CNN or a U-Net style architecture could directly segment the DLPFC in the full MRI volume, potentially improving continuity of the segment and leveraging inter-slice information.
- **Functional Integration:** As noted, integrating functional imaging (rs-fMRI) to create a *connectivity-informed Mask R-CNN* could allow targeting of the DLPFC region with desired network properties (e.g., strongest anticorrelation with subgenual cingulate for depression treatment).
- **Real-Time Guidance:** Adapting the model for real-time neuronavigation – possibly even using camera feed of a person's head aligned to MRI – so that the DLPFC location can be marked on the head in real time for TMS coil positioning. This would involve combining our MRI-based localization with optical tracking systems.
- **Other Brain Regions:** The general approach can be extended to localize other regions of interest for neuromodulation, such as the dorsomedial prefrontal cortex or posterior parietal targets. Each would require its own training data, but the methodology would be similar. Over time, one can imagine a suite of ML models assisting in targeting various brain regions with high precision.

In summary, our Mask R-CNN based approach addresses a clear need in neuroscience for more precise, personalized targeting of brain regions. It demonstrates how state-of-the-art deep learning, when carefully adapted and validated, can translate to practical gains in neuroimaging and brain stimulation. As we overcome the current limitations through further research, such ML-driven tools are poised to become standard components of personalized brain therapy and research.

IX. Conclusion

We presented a novel application of deep learning – using a Mask R-CNN instance segmentation model – to enhance DLPFC localization for neuroimaging and brain stimulation purposes. Our approach achieves automated, personalized identification of the DLPFC on individual MRI scans, overcoming the limitations of traditional methods that ignore anatomical variability. The model demonstrated high accuracy, segmenting the DLPFC with precision comparable to human experts and providing consistent results across individuals. This represents an important step toward **personalized neuromodulation**, where treatments like rTMS can be tailored to a patient's unique brain anatomy, potentially improving efficacy and outcomes.

Crucially, this work highlights that modern machine learning techniques can be successfully brought to bear on longstanding neuroscientific problems – in this case, reliably mapping a functional cortex area for each person. By leveraging a large pre-trained CNN and fine-tuning it on targeted neuroimaging data, we achieved a level of performance that makes clinical translation feasible. The Mask R-CNN model yields an intuitive output (a highlighted brain region) that can readily guide practitioners in real-world settings.

There are still challenges to address, including expanding validation, integrating multimodal data, and demonstrating clinical benefits. However, the framework established here opens several avenues for future research, from multi-modal targeting algorithms to AI-driven guidance systems in brain stimulation. As datasets grow and these models are refined, we anticipate that ML-based brain region localization will become increasingly standard. In the case of DLPFC, this means moving from a one-size-fits-all targeting to a patient-specific approach, embodying the principles of precision medicine in psychiatry.

In conclusion, applying Mask R-CNN to DLPFC localization is a **novel and promising strategy** that bridges machine learning and neuroscience. It provides a tool for personalized targeting that could improve both research investigations (by reducing anatomical variance noise) and clinical interventions (by enhancing treatment precision). With continued development, such techniques will help ensure that each patient's therapy is as *targeted* and effective as possible, based on their own brain's map.

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