A Novel Approach to the Earliest Virtual Dissection of the Ventral Amygdalofugal Pathway In-Vivo

Anurag Nasa[1], Katharina Nagassima[1] , Ezije Ukponu[1], Bharti Kewlani[1], Ashka Shah[1], Thomas Drago[1], Noor Essa[1], Elena Roman[1], Denis Barry[2], Kirk Levins[3], Erik O'Hanlon[1], Veronica O'Keane[1], Darren Roddy[1, 4]

[1] Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin 2, [2] Department of Anatomy, Trinity College Dublin, Dublin 2,
[3] Department of Anaesthetics and Pain Medicine, St Vincent's University Hospital, Dublin 4 ,
[4] Department of Physiology, University College Dublin, Dublin 4

Introduction

The Ventral Amygdalofugal Pathway (VAP) is among the three primary efferents of the amygdala; an almond shaped assembly of nuclei known to be involved in various limbic system processes such as fear, reward, emotional learning and aggression (1). The VAP emanates from the amygdala ventral to the stria terminalis and connects to predominantly the hypothalamus, but also the basal forebrain, nucleus accumbens and the thalamus(2).

While the literature describing the anatomical features of this white matter bundle is scant, the aim of our study was to describe the anatomy of this structure in-vivo by employing advanced neuroimaging techniques.

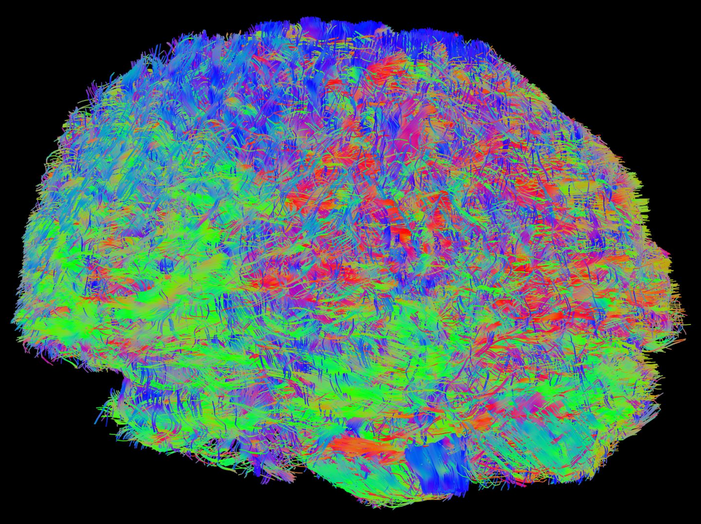

Figure 1: Whole brain tracts, as generated via the Constrained Spherical Deconvolution algorithm

Methods

Diffusion weighted imaging

64 healthy participants were scanned using High Angular Resolution Diffusion Imaging (HARDI) and high-resolution T1 (1mm isotropic) MR imaging at Trinity College Dublin (Phillips, Intega 3T).

Freesurfer 6.0

Three dimensional volumes of the amygdalae and the nucleus accumbens were generated using the automated cortical segmentation protocol within FreeSurfer 6.0 (fig. 2). This protocol of FreeSurfer interrogates contrast differences between substructures using previously defined in-vivo and ex-vivo amygdalae to determine substructure characteristics.

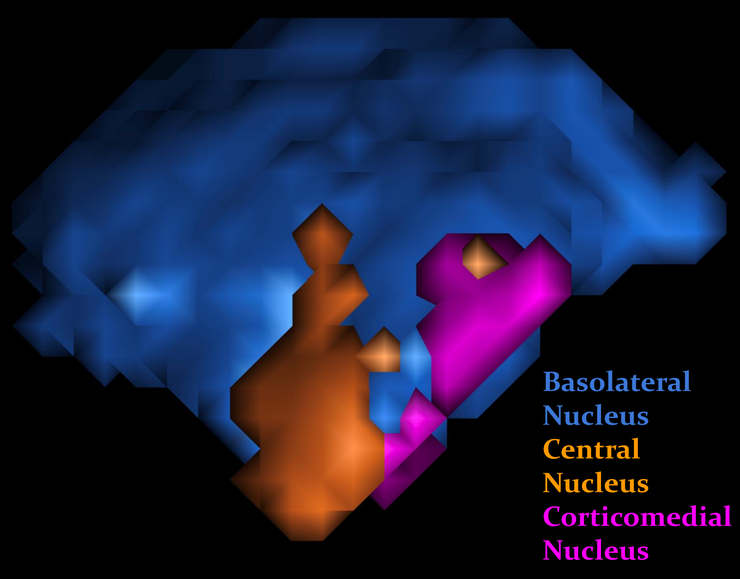

Figure 2: Axial view of nuclear groups within the amygdala, generated using Freesurfer 6.0

DWI Pre-processing

ExploreDTI, a diffusion magnetic imaging toolbox, was utilised for complete pre-processing, modelling and computation of diffusion data. The Constrained Spherical Deconvolution (CSD) algorithm was used to model all potential deterministic streamlines throughout the entire brain (fig. 1).

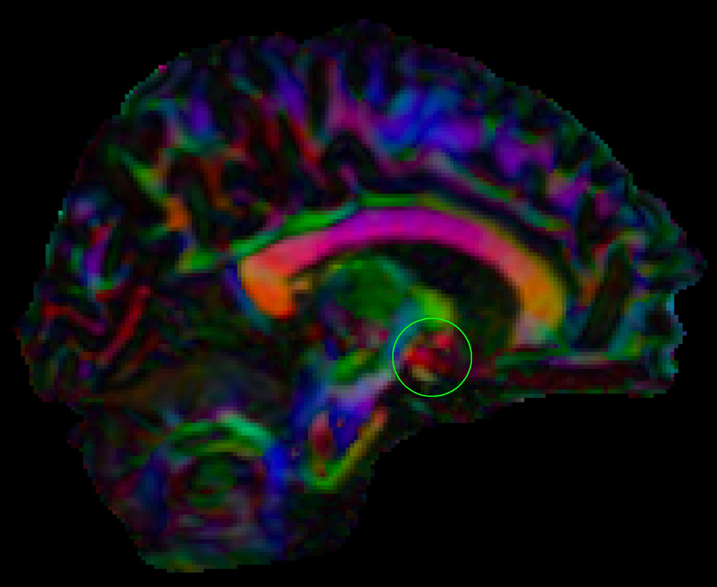

Figure 3: ROI placement on the parasagittal plane of a transformed diffusion weighted image, for isolating the Left VAP

Tractography

The virtual dissection of the tract on each hemisphere can be broadly divided into three main steps: tract localization, branch isolation and whole tract integration.

1. The mask of the amygdala was used as a Region Of Interest (ROI) to delineate tracts which enter the amygdala from the rest of the brain. Then, another two-dimensional ROI was placed in a para-sagittal plane medial to the ipsilateral amygdala around a diffusion image landmark to isolate the Ventral Amygdalofugal Pathway (fig. 3).

2. Each branch from this bundle was isolated manually and individually using an 'OR' Boolean logic operation as a ROI. The branch which goes to the nucleus accumbens was isolated in an automated process, unlike the other branches, using the Freesurfer generated masks as the ROI (fig. 5).

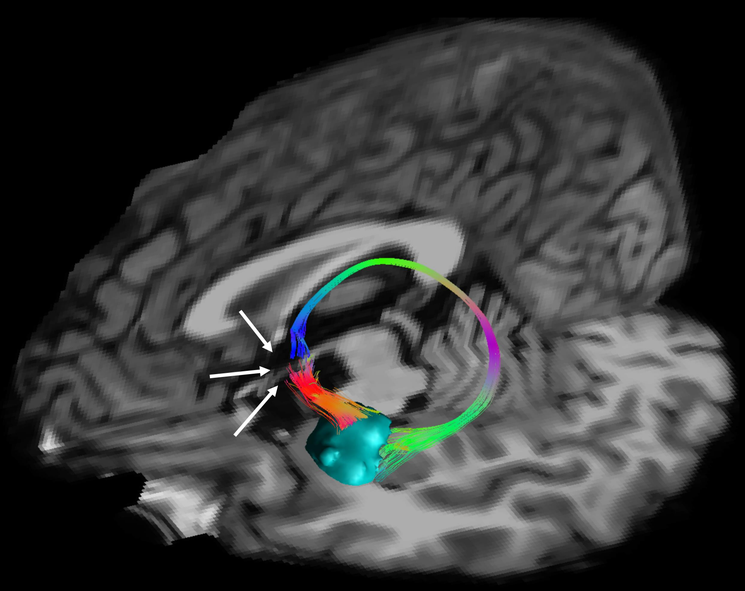

Figure 4: Three dimensional models of the amygdala (cyan), stria terminalis and the branch of the VAP which extends to the hypothalamus. White arrows point at the hypothalamic region.

3. Each of the ROIs which were employed in the isolation of the individual branches were computed in conjunction alongside the pre-processed VAP bundle to isolate the integrated VAP that only contains the branches that are a common factor within the entire sample.

Nucleus Accumbens
Nucleus Accumbens Branch of VAP
Amygdala

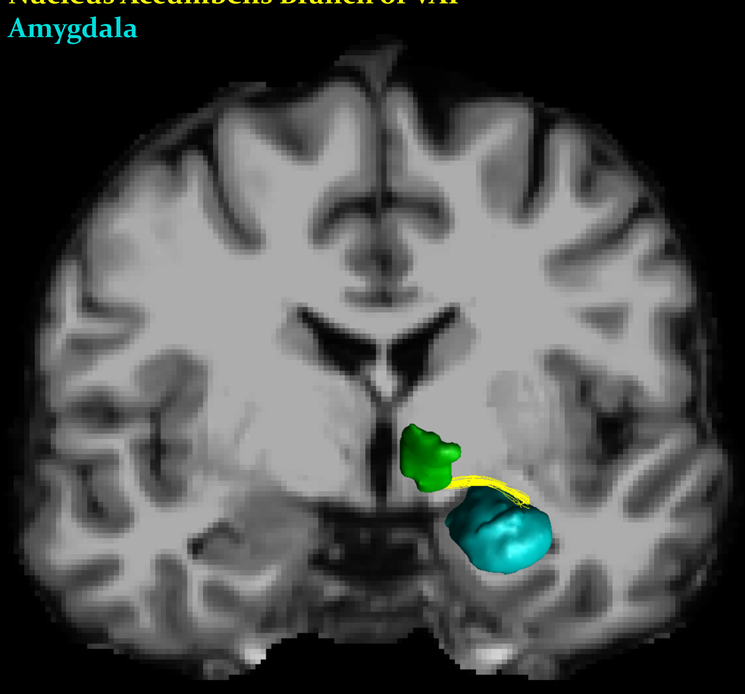

Figure 5: Coronal slice of a T1 MRI image featuring the branch of the VAP which extends to the nucleus accumbens.

Results

The VAP could reliably and consistently be virtually dissected in all participants. Branches which pass through the hypothalamus, basal forebrain and nucleus accumbens were delineated consistently in the whole sample by the raters (fig. 6). The branch which serves the mediodorsal thalamus was found inconsistently.

Ventral Amygdalofugal Pathway
Basal Forebrain Branch
Hypothalamic Branch
Nucleus Accumbens Branch

Amygdala
Basolateral Nucleus
Centromedial nucleus

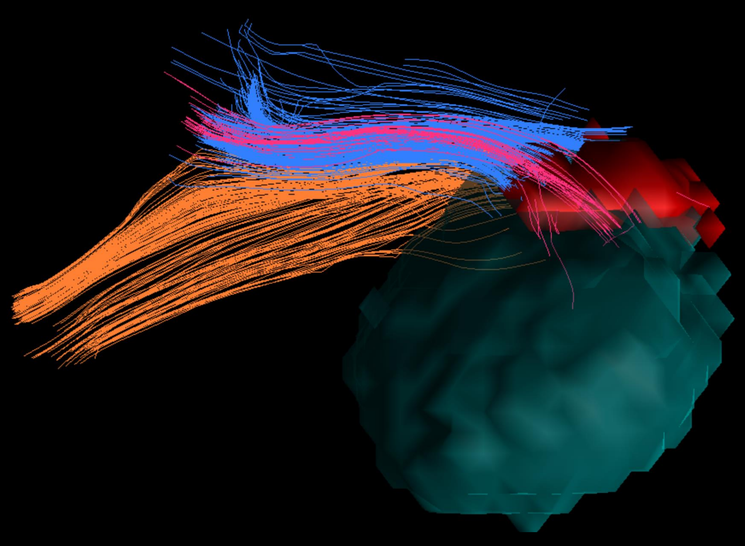

Figure 6: Branches of the VAP as they emanate from the centromedial nucleus of the amygdala

Conclusion

This is the first study to isolate individual branches of the VAP in vivo.

The virtually dissected tracts here can be assessed to determine age related and sex changes. Our protocol may also open avenues for identification of pathologies within components of this enigmatic bundle in neuropsychiatric conditions such as Major Depressive Disorder, Schizophrenia etc.

References:
1. Richardson JS. The amygdala: historical and functional analysis. Acta Neurobiol. Exp. 1973 Jan 1;33(5):623-48.
2. Mori S, Kageyama Y, Hou Z, Aggarwal M, Patel J, Brown T, Miller MI, Wu D, Troncoso JC. Elucidation of white matter tracts of the human amygdala by detailed comparison between high-resolution postmortem magnetic resonance imaging and histology. Frontiers in neuroanatomy. 2017 Mar 14;11:16.