MS Prelim Data K23

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MS preliminary data

Ideas:

Overall: [] demographics - tables made below [] imaging parameters

Aim 1: lesion network mapping [] some picture showing the # of people who are scanned and the # of people with depression. Maybe an adaptation of Syndey's picture somehow. [] mimosa picture [] picture of filtering pipeline [] comparison of some of the histograms for high volume loss similar to prev literature(CN II, slf), not so much in other areas [] results of age analysis [maybe/maybe not, to prove the method works]? [] results of disease in vs outside of depression network (corrected), lead with this? [] results total proportion lost (single p) [] results of dep vs controls across all regions,(uncorrected) [] results of dep vs controls in depression network (uncorrected)

[] prelim network enrichment via spin-testing or just citation? - do I want to validate here or somewhere else with neurosynth maps?

Aim 2: prospective [] power analysis [] CNB (Bart has great Figure 3) [] Goassess

Aim 3 [] Hydra picture [] hydra results from my paper [] acquisition protocol (T1, t2, flair, dwi)

R Markdown

The first chunk here is reading in appropriate data frames and preprocessing. Two big data frames are read in. The first is the demographic, drug, lab info for the MS patients (from the DAC pull). The second is the data frame of fascicle proportion affected for people with good mimosa (# volume affected/total volume of fascicle). The most important preprocessing occurs in a series of mutate commands. These essentially add new columns to the data frame that can later be used. The thrust of these mutate commands is to define who has depression and who does not. Inclusion criteria below:

Inclusion MS Criteria (dataframe read in here has already been filtered down using the exclusions below previously) 1) Scanned under MS protocol (42K) 2) MS Diagnosis (17K) 3) Seen by MS doctor (16K)

Inclusion criteria for Depressed Group 1) Have an ICD10 F3* code (in our sample, people have F32 (depressive episode), F33 (major depressive disorder), and F34 (Persistent mood [affective] disorders)) - there are NO participants with bipolar disorder, manic episode, or unspecified mood/affective disorder) - while participants may have been diagnosed with F06.3 (Depressive disorder due to known physiological condition, with depressive features), they must ALSO have had an F3(2-4) condition 2) Screened positive for depression on PHQ2 or PHQ9 at any point 3) Prescribed antidepressant medications per NAMI website - https://www.nami.org/About-Mental-Illness/Treatments/Mental-Health-Medications

Inclusion criteria for Healthy Group 1) No F* diagnoses 2) At least 1 PHQ2 or PHQ9 with a documented 0 3) Free of psychiatric medications per NAMI website

Exclusions If you received the MS protocol or had a diagnosis of MS but never actually saw an MS provider, we cannot be sure that the diagnosis of MS is truly valid, as it is hard to diagnose anyway. If you did not

have a diagnosis of depression and never completed a PHQ2 or 9, and had no history of medications, we could not safely confirm nor deny the presence of depression. These subjects were excluded from future analyses. We could consider adding these to the healthy group maybe, but not too inclined to do that right now.

Imaging exclusion We are currently only using people who had good MIMOSA (75 or 100). That severely limits our numbers, but that is okay! When we re-QC, we will probably get a lot more into this group.

Final N demographics Depressed: 859 (232 unique) Super clean healthy: 604 (148 unique)

(unique, with good MIMoSA):

	Healthy	Depressed	p	test
n	148	232		
Race (%) Caucasian	108 (73.0)	173 (74.6)	0.821	
Non-caucasian	40 (27.0)	59 (25.4)		
Sex (%) Female	117 (79.1)	199 (85.8)	0.117	
Male	31 (20.9)	33 (14.2)		
Age (mean (SD))	46.57 (12.66)	48.75 (11.75)	0.089	
Depression (%) 1	148 (100.0)	0 (0.0)	<0.001	
2	0 (0.0)	232 (100.0)		
PHQ2 (mean (SD))	0.00 (0.00)	0.58 (1.53)	<0.001	
PHQ9 (mean (SD))	0.00 (NA)	10.43 (9.02)	NA	

Networks

A note on the "depression network." This network was made by Shan Siddiqi in Michael Fox's group by doing a conglomeration of TMS datasets, stroke datasets, Nature Human Behavior 2021 (https://www.nature.com/articles/s41562-021-01161-1). It is a thresholded mask. To use it, I binarized it, and then used it as an ROI and calculated, per fascicle, the proportion of the volume occupied by the fascicle that intersected with the depression mask to the whole volume of the fascicle. Most fascicles were either entirely overlapping or entirely outside the depression mask. We consider the fascicles that had any intersection with the binary depression mask to be within the depression mask, or "indepnet." 47 out of 87 fascicles are in this network. We have an even tighter mask "indepnet_10percent", which indicates that at least 10% of a fascicle's volume intersected or overlapped with the depression mask. 15 are in this network. "in_nondep_net" refers to brain regios that completely avoided the depression network (i.e. had no shared volume of overlap). 40 are in this network

Association fascicles: [1] "AF_L" "AF_R" "C_FPH_L" "C_FPH_R" "C_FP_L" "C_FP_R" "C_PH_L" "C_PHP_L" "C_PHP_R" "C_PH_R"
[11] "C_R_L" "C_R_R" "EMC_L" "EMC_R" "FAT_L" "FAT_R" "IFOF_L" "IFOF_R" "ILF_L" "ILF_R"
[21] "MdLF_L" "MdLF_R" "PAT_L" "PAT_R" "SLF1_L" "SLF1_R" "SLF2_L" "SLF2_R" "SLF3_L" "SLF3_R"
[31] "UF_L" "UF_R" "VOF_L" "VOF_R"

Depression network: [1] "AF_L" "AF_R" "C_PHP_R" "EMC_L" "EMC_R" "FAT_L" "FAT_R" "IFOF_L" "IFOF_R" "ILF_R" "MdLF_L" [12] "MdLF_R" "PAT_L" "PAT_R" "SLF2_L" "SLF2_R" "SLF3_L" "SLF3_R" "V" "AR_R" "CBT_L" "CBT_R"
[23] "CPT_F_L" "CPT_F_R" "CPT_O_L" "CPT_O_R" "CPT_P_L" "CPT_P_R" "CS_A_L" "CS_A_R" "CS_P_L" "CS_P_R" "CS_S_L" [34] "CS_S_R" "CST_L" "CST_R" "DRTT_R" "ML_L" "RST_L" "RST_R" "TR_A_L" "TR_A_R" "TR_P_L" "TR_P_R" [45] "TR_S_L" "TR_S_R" "CC"

Depression 10% network [1] "AF_L" "AF_R" "C_PHP_R" "FAT_L" "FAT_R" "MdLF_L" "MdLF_R" "SLF2_L" "SLF2_R" "SLF3_R" "CBT_L"
[12] "CBT_R" "CPT_O_R" "CS_P_R" "TR_P_R"

Notebook

I start out with a proof of concept analyses, to demonstrate that our lesion filtering works. I create histograms looking at the proportion of volume lost in each fascicle across subjects. We recapitulate earlier work (will need to cite) and show that higher volume loss with our method reflects regions previously known to have higher disease burden.These findings suggest that the streamline filtering approach could be a reasonable approach for this analysis.

Analyses There are two main types of analyses I performed, t.tests (for example, to compare inside versus outside depression network) and linear models (for example, looking at the relationship of depression to each individual fascicle). With respect to T-tests, I assume unequal variance for all. For linear models, I have looked at the first scan (considered Unique for unique empi), the last scan previously (not in this notebook), and mixed models with EMPI as a repeated measure (all at the end of the notebook). I like the unique one the best. The general pattern is to look at the total proportion of volume lost across fascicles, then within depression network, within depression 10% network, and within non depression network. Then, I look at each individual fascicle, as well as separately consider the association fascicles (per DSI studio, these are the ones that connect association cortices).

I attempted to do FDR correction for all analyses where I looked at each of 87 fascicles separately, or bucketed by association network or within depression network. If i was not successful, I included uncorrected ($P<0.05$).

A note about age. I have tried with and without age in these models. Age is so phenomenally strong as an effect (thank goodness) but it actually tends to suck up some of the depression variance so currently it is not in the depression model. Given the age of our participants (range from 20s to 80s), there are I imagine at least two big age effects going on 1) progressive disease and 2) natural (or unnatural aging). Gams would probably be better at looking at this relationship and could probably be its own thing.

And this is only in WM. MS is also associated with GM atrophy. I can only imagine the IMCO paper that could emerge out of looking at the relationship between white matter loss and gray matter atrophy as a function of age. But certainly not for this K! Also sounds like lots of people are interested in this.

I have also looked at sex differences in individual fascicles. Underwhelming right now.

Results Depression group: 232 with depression, 148 healthy. PHQ2 Looking at each person's first scan:

```
*Age effects:
  -Age mean 47 (range 20-83).
  -Almost everything corrects (54 out of 87 fascicles, 25 in association network)
  -Take home - as expected, the older you are, the worse white matter fascicle invovlement you have

*Sex effects:
  - In the final good MIMoSA group, there were 64 unique males and 316 unique females, 83% women
  - Individual fascicle results underwhelming, only 3 regions meet P<0.05 (unc), SCP, CPT_O_R, OR_R
  - no association or within dep network findings
  - Analyses to consider at a later date
    [] looking at overall fascicle prop lost (rather than inidiv region)
    [] dep * sex
    [] some sort of matching

*Depression over all fascicles:
  - The exciting news of the day! With our new depression group (moving the meds people), we have findi
  - total proportion lost - p = 0.049, depressed (27%) more loss than healthy(24%)
  - total proportion lost within depression network - trend (0.059) between depressed (35%) and healthy
  - total proportion lost within depression 10% network - p =  0.049 (depressed (33%) have more loss th
  - total proportion lost outside depression network- p = 0.037 (depressed (18%) more than healthy(16%)
  - take home - people with a lifetime history of depression have more disease than nondepressed indivi
```

```
*MS disease and depression network overlap:
  - Ms disease within depression network (35%) versus outside (17%), p < 2.2* 10^-16
  - MS disease within depression 10% network (31%) versus outside (17%), p < 2.2 * 10^-16
  - Linear Regressions (essentially matching t tests above):
     +depressed v healthy within dep network in (p = 0.061);
     +dep vs healthy within dep 10% (p = 0.049);
     +dep vs healthy within non dep network (p = 0.037)
  - Take home: Multiple sclerosis white matter lesions co-locate with brain regions previously associat
*Depression by individual fascicle:
  - Nothing corrects at this time, unfortunately.
  - P<0.05, uncorrected findings (* indicates association network):
      -AF_R 0.01168289  *
      -FAT_R    0.01828607 *
      -SLF2_R   0.01901378 *
      -VOF_R    0.04741569 *
      -CPT_F_R  0.02887163
      -CPT_O_L  0.02238344
      -CPT_P_R  0.02053104
      -CS_S_R   0.03783654
      -DRTT_R   0.00695066
      -ML_R 0.02511932
Fascicle loss x PHQ9:
 - future analysis?
```

Limitations/Future directions

All diagnostic info is obtained from EMR fields, not notes, nor direct chart review. We do not know if patients are relapsing/remiting, nor do we know their active depression status. Through careful review, though patients sometimes have many phq2s listed, they are always identical.

It would be great if we also had better dimensional scores. The PHQ2s are largely 0s, and the lack of spread makes interpretation really challenging. Though the PHQ9s definitely have better spread, there just aren't many of them. Doing really good cognitive and clinical phenotyping, or even getting a different or better set of measures into the MS clinic would be ideal (Aim 2).

With respect to networks, we have used the "depression" one from Harvard because I was inspired by the lesion network mapping work. However, the mask is pretty broad, covering and strongly overlapping with the executive network. There is bias toward having regions that functionally connect with the L DLPFC b/c it is a TMS target. We are considering neurosynth as a possible place to look at different depression masks.

Interestingly, a key topic at the ACTRIMS 2022 conference was psychiatric comorbidity. Though we are focusing on depression, it sounds like anxiety is just as bad if not worse or more highly comorbid with MS. Would be worth considering not only a DSM breakdown but dimensionally looking at internalizing disorders for the K. Also more in line with rdoc but would require changing aims a bit.

Future analyses: age x dep, sex x dep

```r
homedir <- "/Users/eballer/BBL/msdepression/"

data <- read.csv(paste0(homedir, "/data/drugs_data/parsable_msdepression.csv"), sep = ",", header = TRU

columns_to_make_integer <- c("ACCESSION_NUM", "PAT_AGE_AT_EXAM","MRI_ENC_AGE","CURRENT_AGE","hemoglobin

##########################
### some preprocessing ###
##########################
```

```r
#we need to keep scans from people seen by an MS provider (n = 17067) who have an MS diagnostic code (n
#we make a bunch of columns from character to integer, binarize sex and race, and put date into a nice

#goal is to keep people who were seen by
 data_empi_acc_f_phq <- data %>%
   mutate(across(.cols = columns_to_make_integer, .fns = as.integer)) %>%
   mutate(sex_binarized = ifelse(SEX == "MALE", 1, 2)) %>%
   mutate(osex = ordered(sex_binarized,levels = c(1,2), labels = c("Male","Female"))) %>%
   mutate(race_binarized = ifelse(RACE == "WHITE", 1, 2)) %>%
   mutate(orace = ordered(race_binarized,levels = c(1,2), labels = c("White","Non-white"))) %>%
   mutate(EXAM_DATE = as.Date(BEGIN_EXAM_DTTM, format = "%m/%d/%y")) %>%
   mutate(EXAM_DATE = gsub(EXAM_DATE, pattern = "-", replacement = "")) %>%
   mutate(EMPI = as.factor(EMPI)) %>%
   mutate(On.Psych.Meds = ifelse(On.Psych.Meds == "True", 1, 0)) %>%
   mutate(On.Antidepressants = ifelse(On.Antidepressants == "True", 1, 0)) %>%
   mutate(Has.PHQ2 = ifelse(Has.PHQ2 == "True", 1, 0)) %>%
   mutate(Has.PHQ9 = ifelse(Has.PHQ9 == "True", 1, 0)) %>%
   mutate(Has.depdx = ifelse(grepl("F3", ICD10), 1, 0)) %>%
   mutate(PHQ.2_modsev_dep_sxs = ifelse((!is.na(PHQ.2) & PHQ.2 >= 3), 1, 0)) %>%
   mutate(PHQ.9_modsev_dep_sxs = ifelse((!is.na(PHQ.9) & PHQ.9 >= 10), 1, 0)) %>%
   mutate(PHQ.2_mild_dep_sxs = ifelse((!is.na(PHQ.2) & PHQ.2 > 0 & PHQ.2 < 3), 1, 0)) %>%
   mutate(PHQ.9_mild_dep_sxs = ifelse((!is.na(PHQ.9) & PHQ.9 > 0 & PHQ.9 < 10), 1, 0)) %>%
   mutate(PHQ.2_zero = ifelse((!is.na(PHQ.2) & PHQ.2 == 0), 1, 0)) %>%
   mutate(PHQ.9_zero = ifelse((!is.na(PHQ.9) & PHQ.9 == 0), 1, 0)) %>%
   mutate(dep_by_dx_phq = ifelse((Has.depdx | PHQ.2_modsev_dep_sxs | PHQ.9_modsev_dep_sxs),1,0)) %>%
   mutate(dep_by_dx_phq_antidep = ifelse((Has.depdx | On.Antidepressants | PHQ.2_modsev_dep_sxs | PHQ.9
   mutate(true_healthy = ifelse((!Has.depdx & !On.Psych.Meds & (PHQ.2_zero | PHQ.9_zero)), 1, 0)) %>%
   mutate(dep_by_dx_phq_meds_healthy_phq0_no_psych_meds = ifelse(dep_by_dx_phq_antidep | true_healthy,
   rowwise(ACCESSION_NUM) %>%
   mutate(depGroupVar =
            sum(c(dep_by_dx_phq_meds_healthy_phq0_no_psych_meds,dep_by_dx_phq_antidep))) %>%#you get an
   ungroup()
```

```
## Note: Using an external vector in selections is ambiguous.
## i Use ‘all_of(columns_to_make_integer)‘ instead of ‘columns_to_make_integer‘ to silence this message
## i See <https://tidyselect.r-lib.org/reference/faq-external-vector.html>.
## This message is displayed once per session.

## Warning in mask$eval_all_mutate(quo): NAs introduced by coercion

## Warning in mask$eval_all_mutate(quo): NAs introduced by coercion

## Warning in mask$eval_all_mutate(quo): NAs introduced by coercion

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```
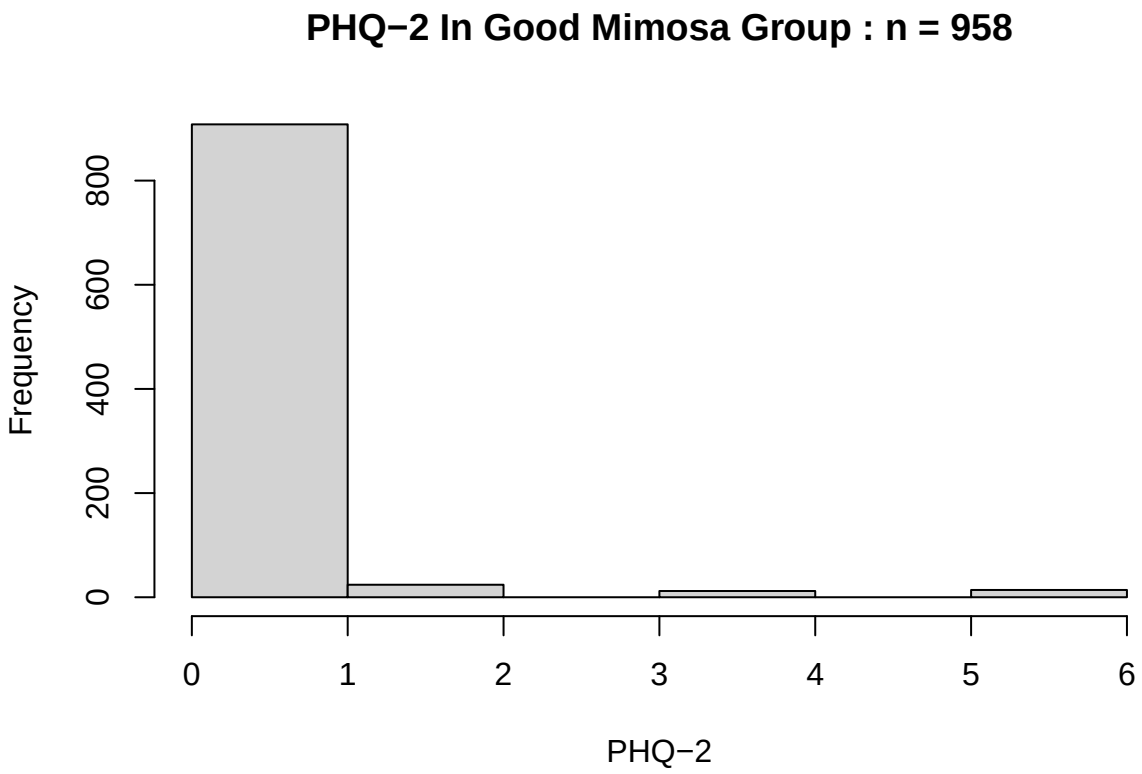

```
## Warning in mask$eval_all_mutate(quo): NAs introduced by coercion
```

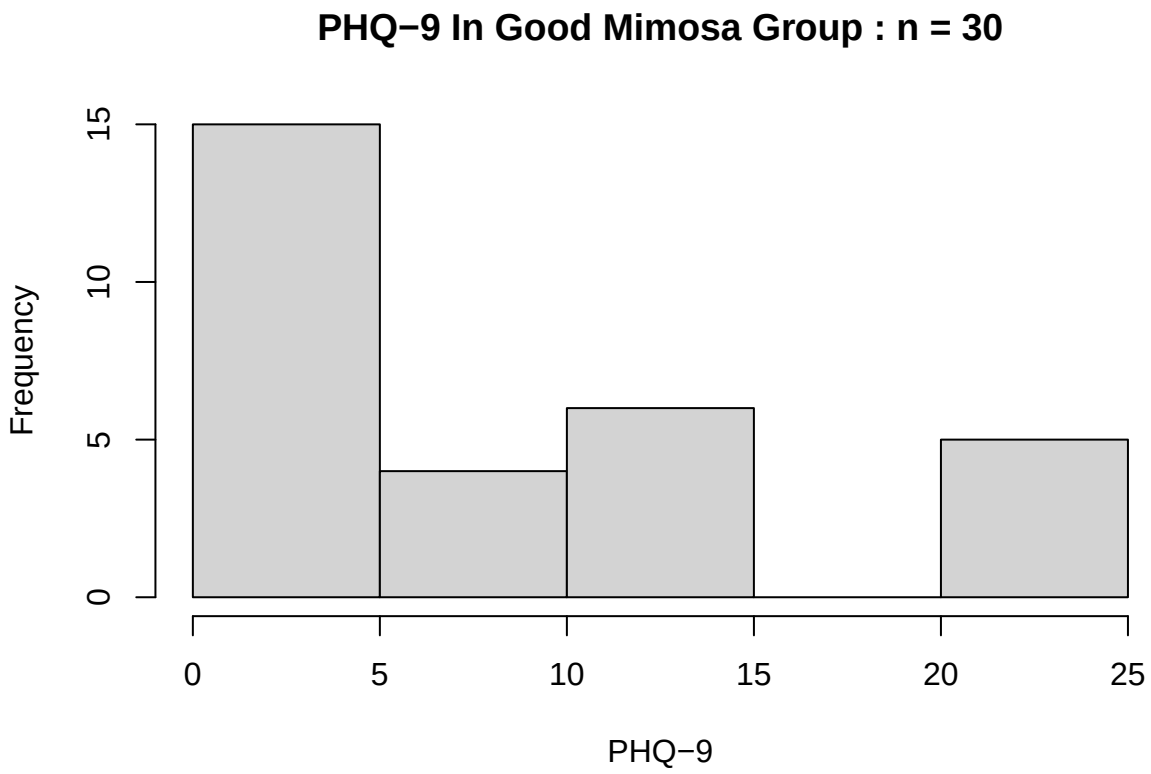
```
#############################################################
#             Read in Fascicle info                 #
#############################################################

fascicle_proportions <- read.csv(paste0(homedir, "/results/fascicle_volumes_all_subjects_roi_n2336.csv"

#fascicle names are contained in all but the first 2 columns of the fascicle_proportions df
fascicle_names <- names(fascicle_proportions[3:dim(fascicle_proportions)[2]])

write.table(fascicle_names,"/Users/eballer/BBL/msdepression/templates/dti/HCP_YA1065_tractography/fasci


########
#fascicle volumes in depression network
########
fascicle_volumes_dep <- read.csv(paste0(homedir, "results/streamline_volume_within_dep_network.csv"), h

#add column to indicate whether does not meet criteria for inclusion in dep mask (0), any overlapping v
fascicle_volumes_dep_network <- fascicle_volumes_dep %>%
  replace(is.na(.), 0) %>%
  mutate(inDepMask=case_when(prop_in_mask == 0 ~ 0, (prop_in_mask > 0 & prop_in_mask < 0.1) ~ 1, prop_i

write.table(fascicle_volumes_dep_network, paste0(homedir,  "/templates/dti/HCP_YA1065_tractography/fasc

fascicle_names_nondep_network<- fascicle_volumes_dep_network$fascicle[which(fascicle_volumes_dep_networ

fascicle_names_dep_network_all <- fascicle_volumes_dep_network$fascicle[which(fascicle_volumes_dep_netw

#fascicle_names_dep_network_all <- fascicle_volumes_dep_network$fascicle[which(fascicle_volumes_dep_net
#write.table(fascicle_names_dep_network_all,"/Users/eballer/BBL/msdepression/templates/dti/HCP_YA1065_t

fascicle_names_dep_network_10_percent <- fascicle_volumes_dep_network$fascicle[which(fascicle_volumes_d
#write.table(fascicle_names_dep_network_10_percent,"/Users/eballer/BBL/msdepression/templates/dti/HCP_Y

#fascicle_mapping, returns numerical mapping as well as names of tracts, and whether in or out of dep n
fascicle_bundle_mapping <- get_fascicle_bundle_mapping()

#############################################################
#             Merge with data_empi                  #
#############################################################
df_demo_and_fascicles <- merge(data_empi_acc_f_phq, fascicle_proportions, by = c("EMPI", "EXAM_DATE")) 
```

```
## Warning in `[<-.factor`(`*tmp*`, ri, value = c(1000005881, 1000005881,
## 1000008469, : invalid factor level, NA generated
```

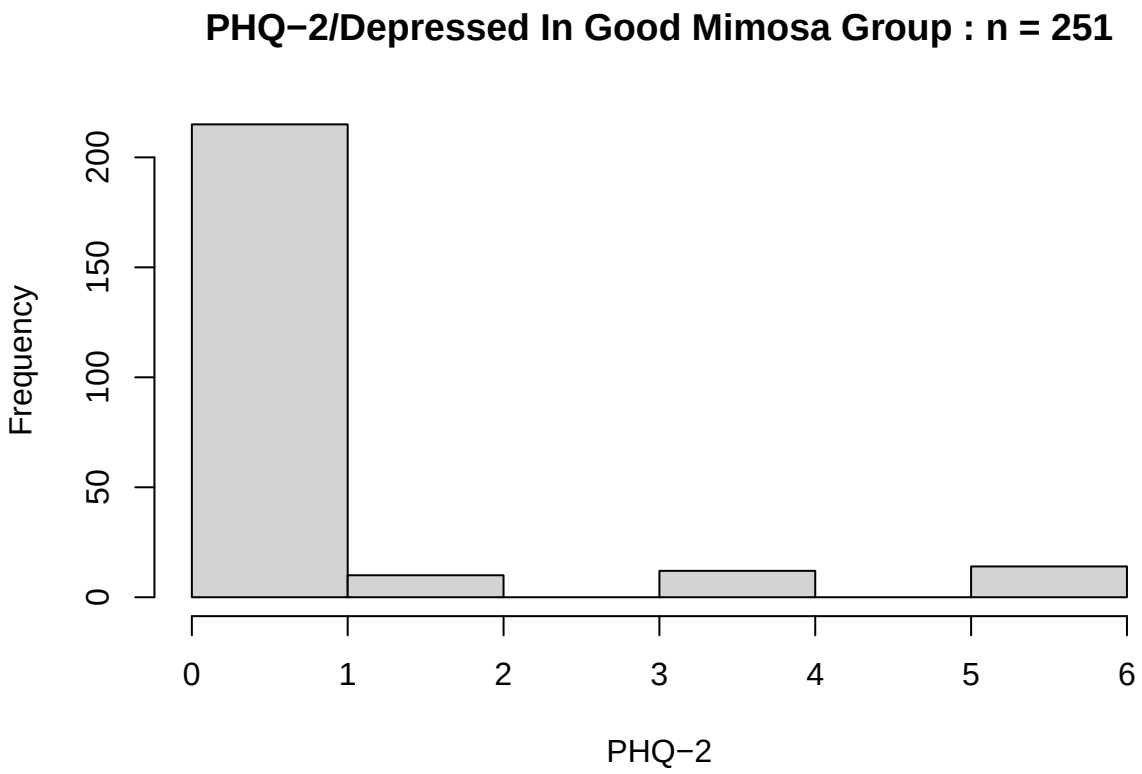
```
#############################################################
#                 Histos                            #
#############################################################
##### Histograms for PHQ2/9 healthy and depressed

hist(df_demo_and_fascicles$PHQ.2[which(!is.na(df_demo_and_fascicles$PHQ.2))], main = paste0("PHQ-2 In G
```



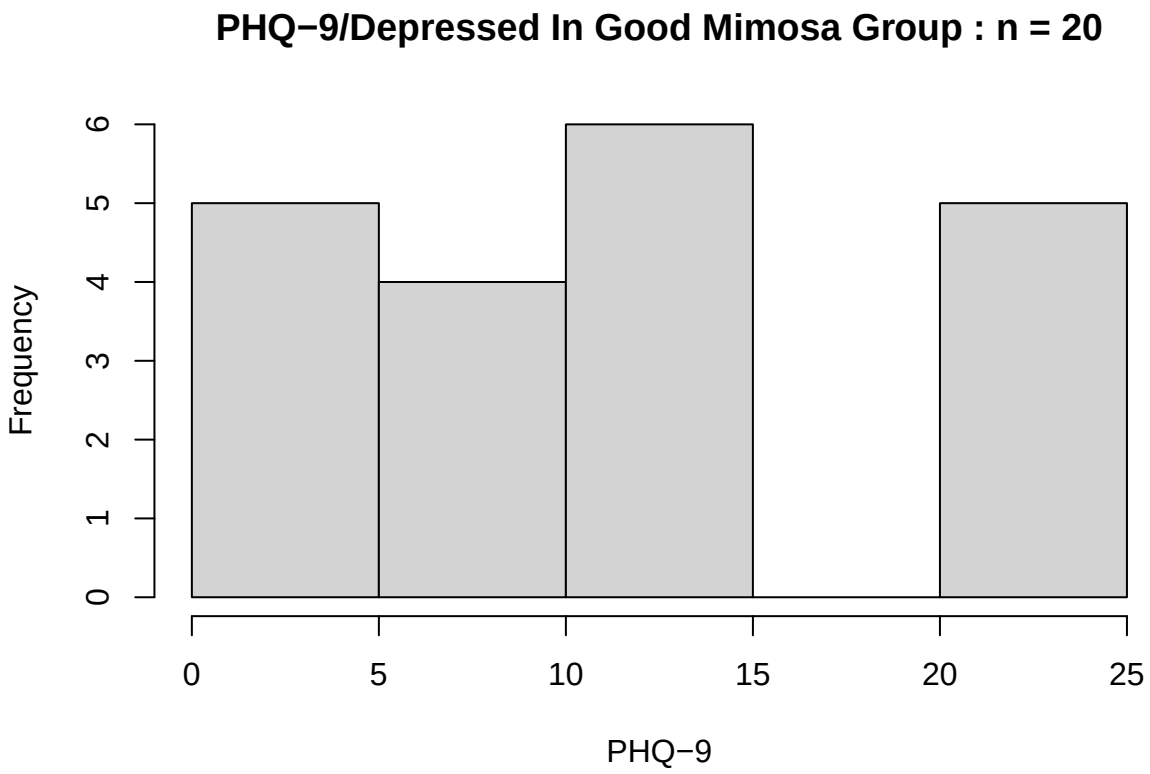

```
hist(df_demo_and_fascicles$PHQ.9[which(!is.na(df_demo_and_fascicles$PHQ.9))], main = paste0("PHQ-9 In G
```



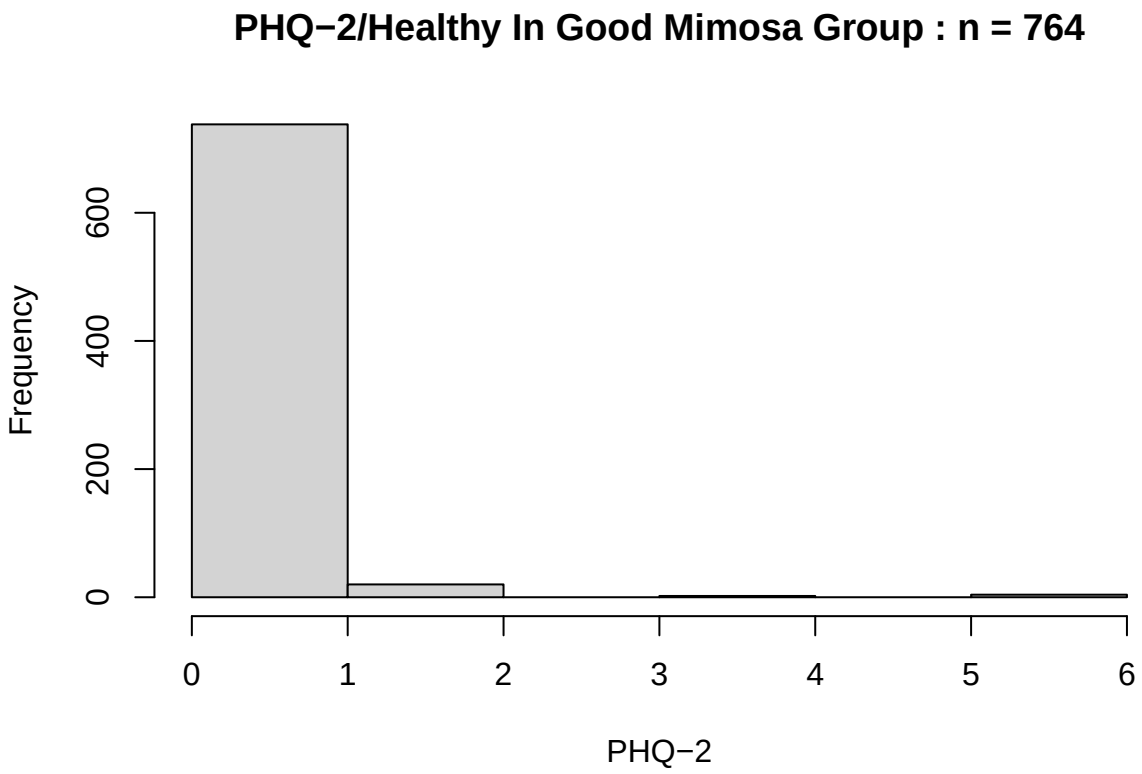

```
phq2_and_dep <- df_demo_and_fascicles %>% filter(depGroupVar == 2) %>% drop_na(PHQ.2)
phq9_and_dep <- df_demo_and_fascicles %>% filter(depGroupVar == 2) %>% drop_na(PHQ.9)
phq2_and_healthy <- df_demo_and_fascicles %>% filter(Has.depdx == 0) %>% drop_na(PHQ.2)
phq9_and_healthy <- df_demo_and_fascicles %>% filter(Has.depdx == 0) %>% drop_na(PHQ.9)

hist(phq2_and_dep$PHQ.2, main = paste0("PHQ-2/Depressed In Good Mimosa Group : n = ", dim(phq2_and_dep)
```



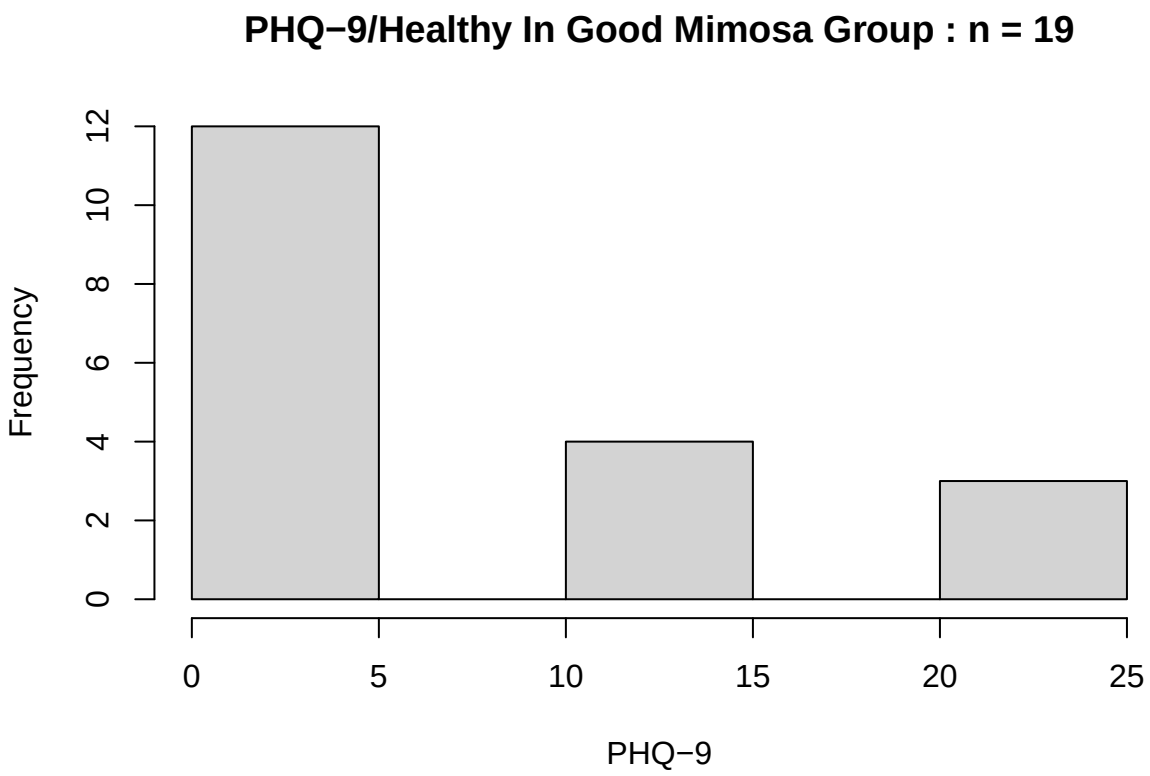

```
hist(phq9_and_dep$PHQ.9, main = paste0("PHQ-9/Depressed In Good Mimosa Group : n = ", dim(phq9_and_dep)
```




```
hist(phq2_and_healthy$PHQ.2, main = paste0("PHQ-2/Healthy In Good Mimosa Group : n = ", dim(phq2_and_hea
```




```
hist(phq9_and_healthy$PHQ.9, main = paste0("PHQ-9/Healthy In Good Mimosa Group : n = ", dim(phq9_and_hea
```



Depression versus healthy analysis

```
#this will display a demographics table comparing age, race, sex between healthy and depressed groups,

make_demographics_table_ms(data_frame = data_empi_acc_f_phq)
```

```
##                   Stratified by Depression
##                    level         0              1              2
##   n                                 9452           2608           4770
##   Race (%)         Caucasian      6885 ( 72.8)   1836 ( 70.4)   3453 ( 72.4)
##                    Non-caucasian  2567 ( 27.2)    772 ( 29.6)   1317 ( 27.6)
##   Sex (%)          Female         6860 ( 72.6)   2005 ( 76.9)   3878 ( 81.3)
##                    Male           2592 ( 27.4)    603 ( 23.1)    892 ( 18.7)
##   Age (mean (SD))                46.74 (12.16)  45.95 (12.66)  48.47 (12.12)
##   Depression (%)   0              9452 (100.0)      0 (  0.0)      0 (  0.0)
##                    1                 0 (  0.0)   2608 (100.0)      0 (  0.0)
##                    2                 0 (  0.0)      0 (  0.0)   4770 (100.0)
##   PHQ2 (mean (SD))                 0.50 (0.75)    0.00 (0.00)    0.61 (1.44)
##   PHQ9 (mean (SD))                 5.11 (2.60)    0.00 (0.00)   10.99 (6.77)
##                   Stratified by Depression
##                    p      test
##   n
##   Race (%)          0.047
##
```

```
##   Sex (%)          <0.001
##
##   Age (mean (SD))  <0.001
##   Depression (%)   <0.001
##
##
##   PHQ2 (mean (SD)) <0.001
##   PHQ9 (mean (SD)) <0.001
```

```
df_unique_empi <- data_empi_acc_f_phq %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()

make_demographics_table_ms(data_frame = df_unique_empi)
```

```
##                   Stratified by Depression
##                    level         0              1              2
##   n                                 2183            488           1066
##   Race (%)         Caucasian      1503 ( 68.9)    312 ( 63.9)    750 ( 70.4)
##                    Non-caucasian   680 ( 31.1)    176 ( 36.1)    316 ( 29.6)
##   Sex (%)          Female         1596 ( 73.1)    371 ( 76.0)    864 ( 81.1)
##                    Male            587 ( 26.9)    117 ( 24.0)    202 ( 18.9)
##   Age (mean (SD))                 45.14 (12.37)  44.33 (12.78)  47.43 (12.28)
##   Depression (%)   0              2183 (100.0)      0 (  0.0)      0 (  0.0)
##                    1                 0 (  0.0)    488 (100.0)      0 (  0.0)
##                    2                 0 (  0.0)      0 (  0.0)   1066 (100.0)
##   PHQ2 (mean (SD))                 0.54 (0.76)    0.00 (0.00)    0.73 (1.55)
##   PHQ9 (mean (SD))                 5.45 (2.70)    0.00 (0.00)   11.37 (6.84)
##                   Stratified by Depression
##                    p      test
##   n
##   Race (%)          0.038
##
##   Sex (%)          <0.001
##
##   Age (mean (SD))  <0.001
##   Depression (%)   <0.001
##
##
##   PHQ2 (mean (SD)) <0.001
##   PHQ9 (mean (SD))  0.001
```

```
df_just_healthy_and_depressed <- df_unique_empi %>% filter(depGroupVar != 0)

make_demographics_table_ms(data_frame = df_just_healthy_and_depressed)
```

```
##                   Stratified by Depression
##                    level         1              2              p      test
##   n                                 488           1066
##   Race (%)         Caucasian      312 ( 63.9)    750 ( 70.4)   0.014
##                    Non-caucasian   176 ( 36.1)    316 ( 29.6)
```

```
##   Sex (%)          Female          371 ( 76.0)    864 ( 81.1)   0.027
##                    Male            117 ( 24.0)    202 ( 18.9)
##   Age (mean (SD))                44.33 (12.78)  47.43 (12.28)  <0.001
##   Depression (%)   1               488 (100.0)      0 (  0.0)  <0.001
##                    2                 0 (  0.0)   1066 (100.0)
##   PHQ2 (mean (SD))                 0.00 (0.00)    0.73 (1.55)   <0.001
##   PHQ9 (mean (SD))                 0.00 (0.00)   11.37 (6.84)    0.006
```

```
#just people with good mimosa
df_good_mimosa <- df_demo_and_fascicles %>% filter(depGroupVar != 0)
make_demographics_table_ms(data_frame = df_good_mimosa)
```

```
##                    Stratified by Depression
##                     level         1              2              p      test
##   n                                  604            859
##   Race (%)          Caucasian       459 ( 76.0)    658 ( 76.6)   0.836
##                     Non-caucasian   145 ( 24.0)    201 ( 23.4)
##   Sex (%)           Female          484 ( 80.1)    719 ( 83.7)   0.091
##                     Male            120 ( 19.9)    140 ( 16.3)
##   Age (mean (SD))                 46.17 (12.23)  48.39 (11.94)   0.001
##   Depression (%)    1               604 (100.0)      0 (  0.0)  <0.001
##                     2                 0 (  0.0)    859 (100.0)
##   PHQ2 (mean (SD))                  0.00 (0.00)    0.64 (1.60)   <0.001
##   PHQ9 (mean (SD))                  0.00 (0.00)   10.20 (8.15)    0.099
```

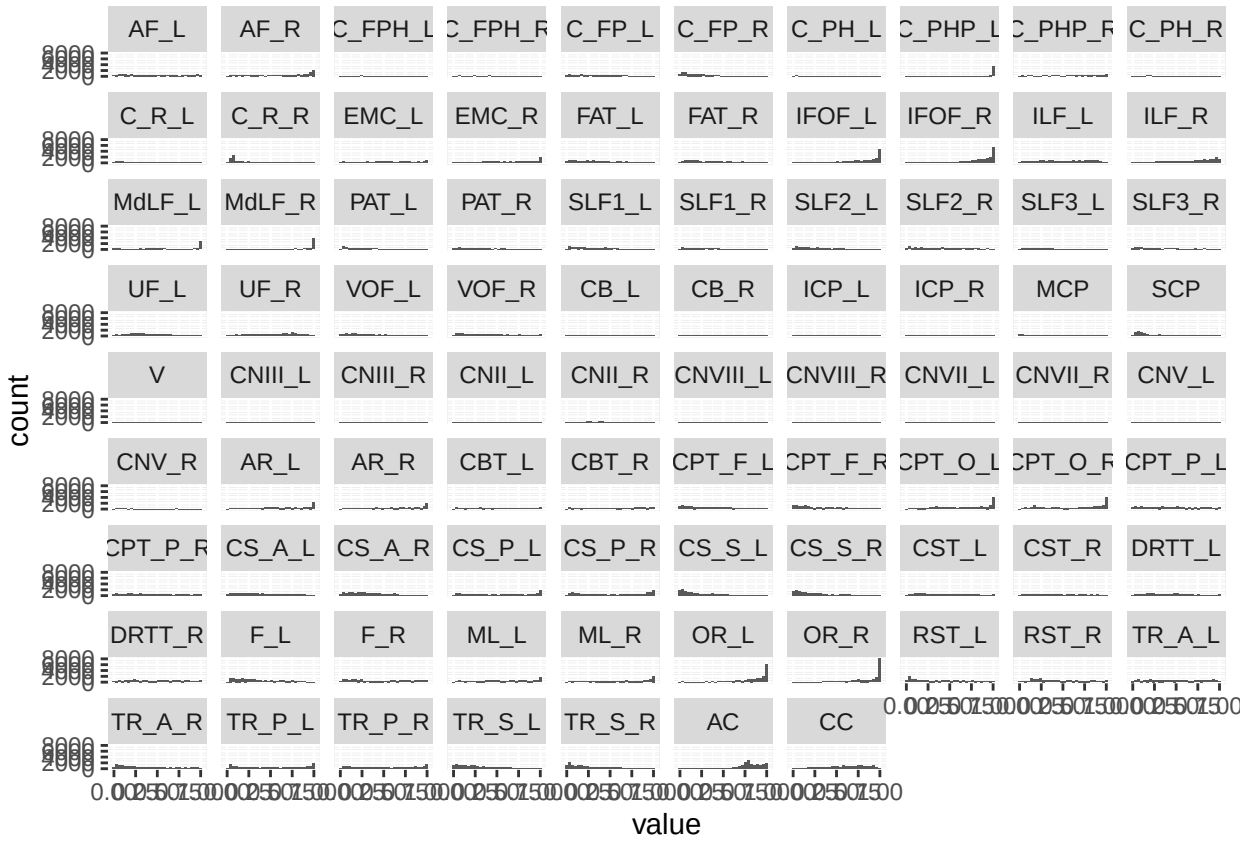
```
df_good_mimosa_unique <- df_demo_and_fascicles %>%
  filter(depGroupVar != 0) %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()
make_demographics_table_ms(data_frame = df_good_mimosa_unique)
```

```
##                    Stratified by Depression
##                     level         1              2              p      test
##   n                                  148            232
##   Race (%)          Caucasian       108 ( 73.0)    173 ( 74.6)   0.821
##                     Non-caucasian    40 ( 27.0)     59 ( 25.4)
##   Sex (%)           Female          117 ( 79.1)    199 ( 85.8)   0.117
##                     Male             31 ( 20.9)     33 ( 14.2)
##   Age (mean (SD))                 46.57 (12.66)  48.75 (11.75)   0.089
##   Depression (%)    1               148 (100.0)      0 (  0.0)  <0.001
##                     2                 0 (  0.0)    232 (100.0)
##   PHQ2 (mean (SD))                  0.00 (0.00)    0.58 (1.53)   <0.001
##   PHQ9 (mean (SD))                  0.00 (NA)     10.43 (9.02)       NA
```

```
#this section creates histograms looking at the proportion of volume lost in each fascicle across subje
#we recapitulate earlier work and show that higher volume loss with our method reflects regions previou
#These findings suggest that the streamline filtering approach could be a reasonable approach for this

#have to pull out just the pieces I'm interested in
just_dep_and_empi <- subset(data_empi_acc_f_phq, select = c("EMPI", "depGroupVar"))
```

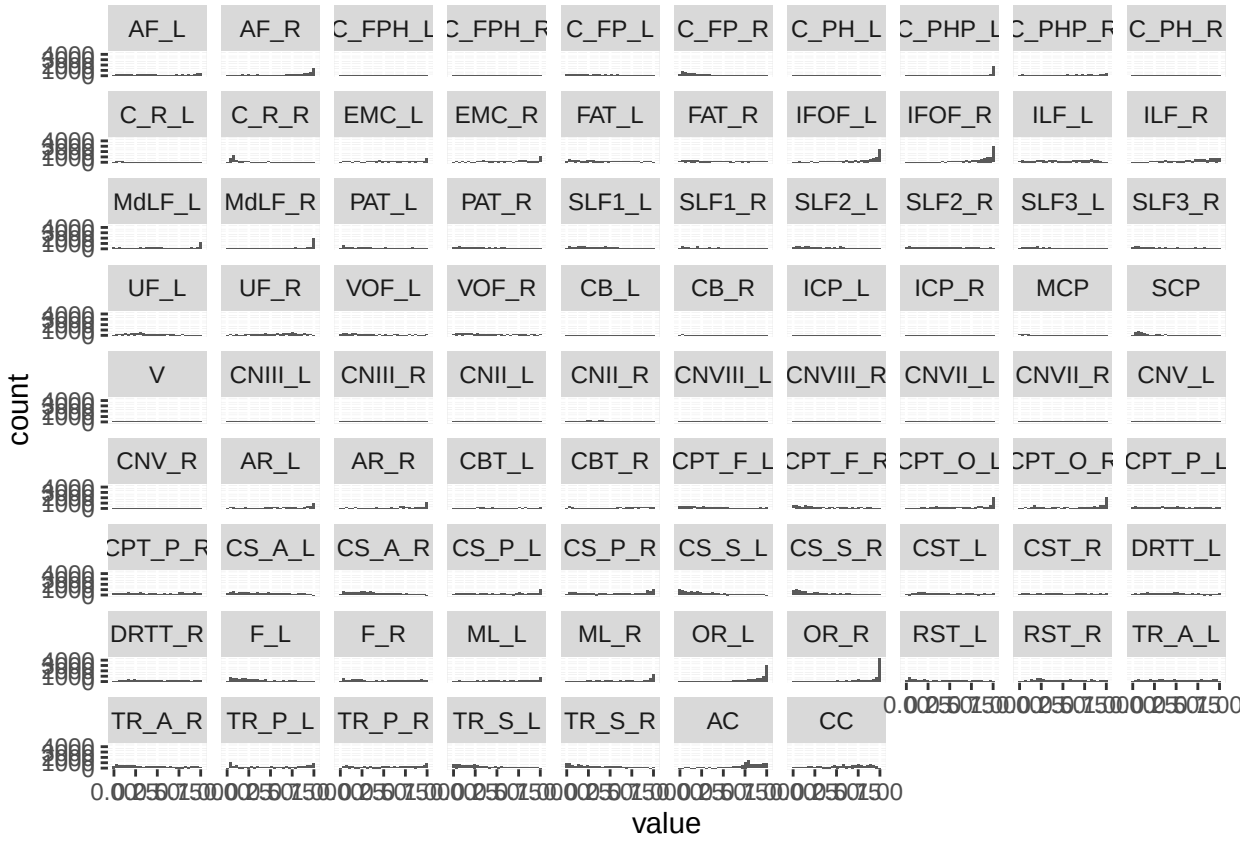
```
added_dep_to_fascicles <- merge(just_dep_and_empi, fascicle_proportions, by = c("EMPI"))
melted_df <- melt(added_dep_to_fascicles, id.vars = c("EMPI", "EXAM_DATE", "depGroupVar"))

#exclude regions where there was no lesion at all
lesioned <- subset(melted_df, value > 0)

#only include people in healthy or depressed group
lesioned_dx <- subset(lesioned, depGroupVar != 0)

#separate out healthy and depressed
healthy <- subset(lesioned, depGroupVar == 1)
depressed <- subset(lesioned, depGroupVar == 2)

q<-ggplot(lesioned, aes(x=value, fill=depGroupVar)) + geom_histogram() + facet_wrap(~variable)
r<-ggplot(lesioned_dx, aes(x=value, fill=depGroupVar)) + geom_histogram() + facet_wrap(~variable)
r_color<-ggplot(lesioned_dx, aes(x=value, color=factor(depGroupVar))) + geom_histogram() + facet_wrap(~
x<-ggplot(lesioned, aes(x=value)) + geom_histogram() + facet_wrap(~variable)
y<-ggplot(healthy, aes(x=value)) + geom_histogram() + facet_wrap(~variable)
z<-ggplot(depressed, aes(x=value)) + geom_histogram() + facet_wrap(~variable)

print(q)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



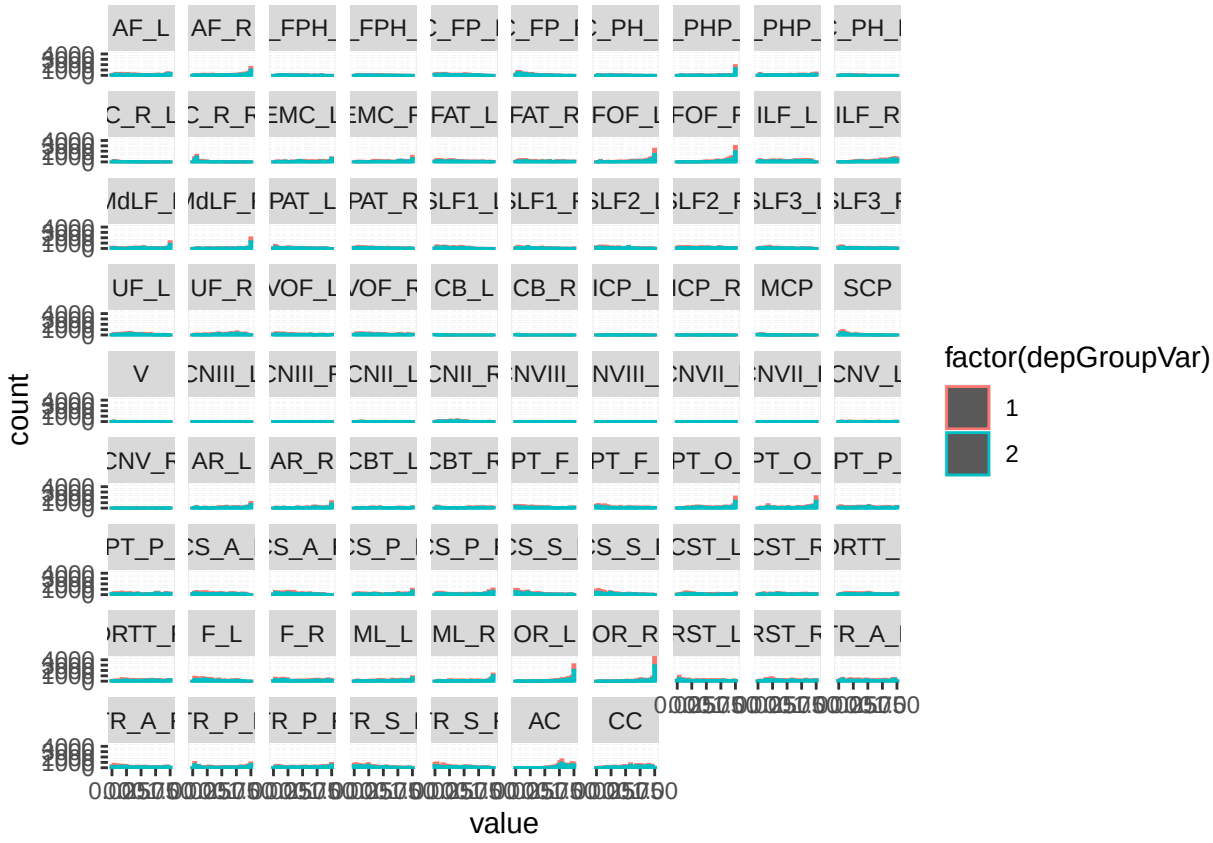
```
print(r)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



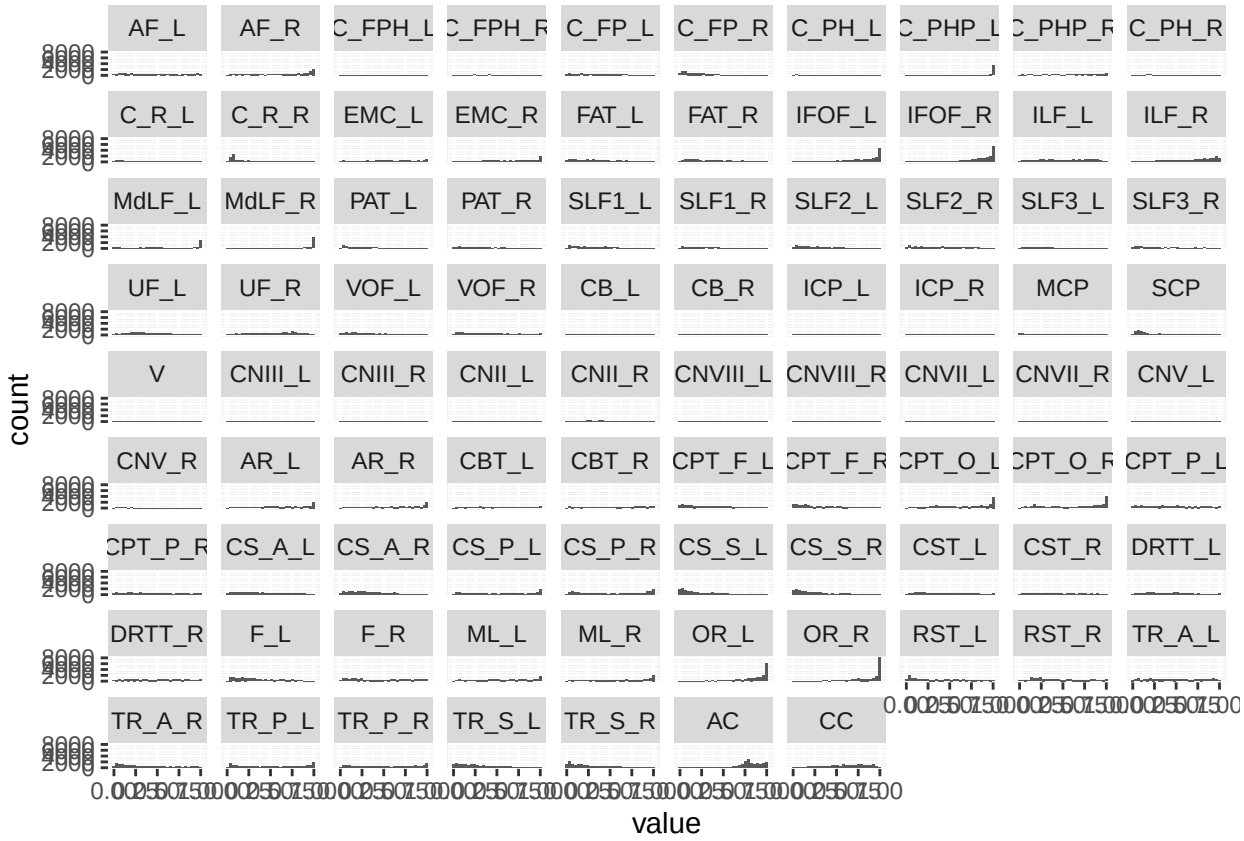

```
print(r_color)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



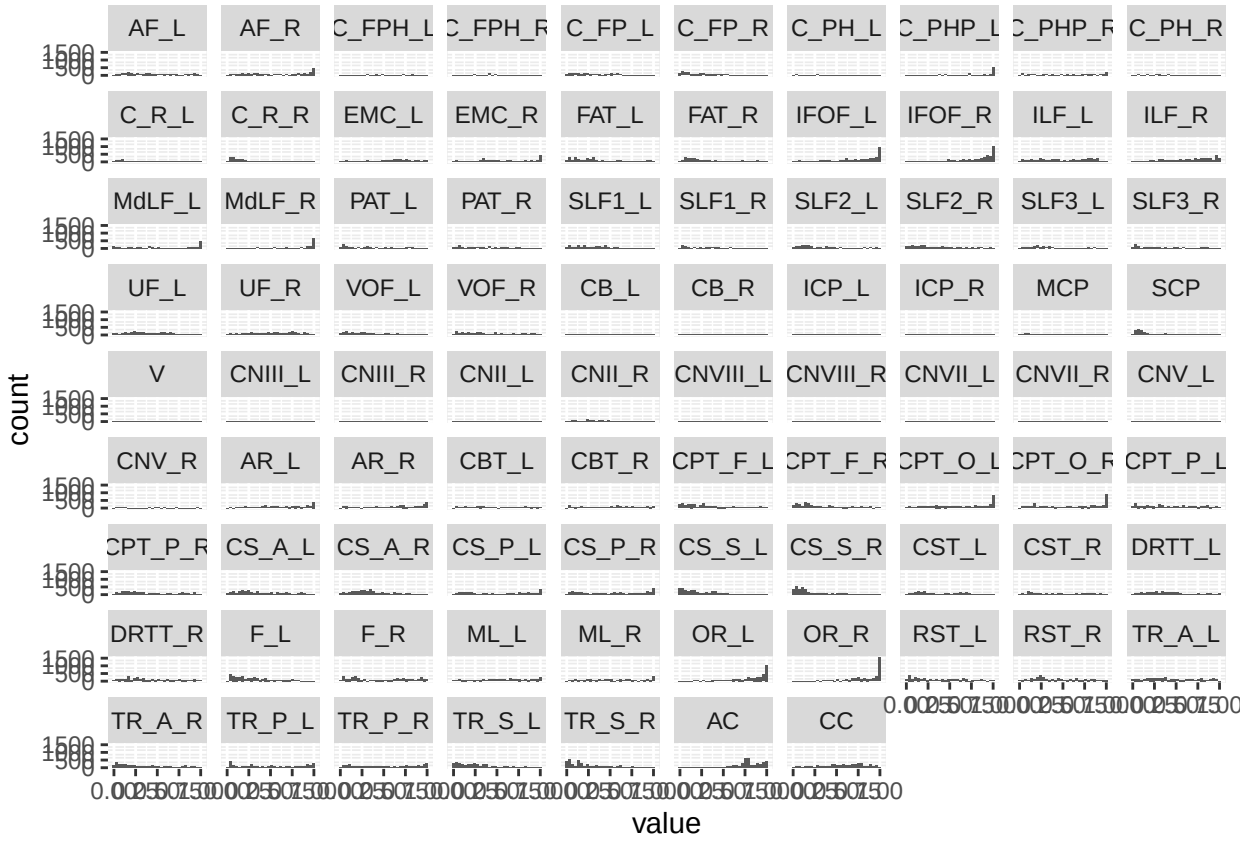

```
print(x)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



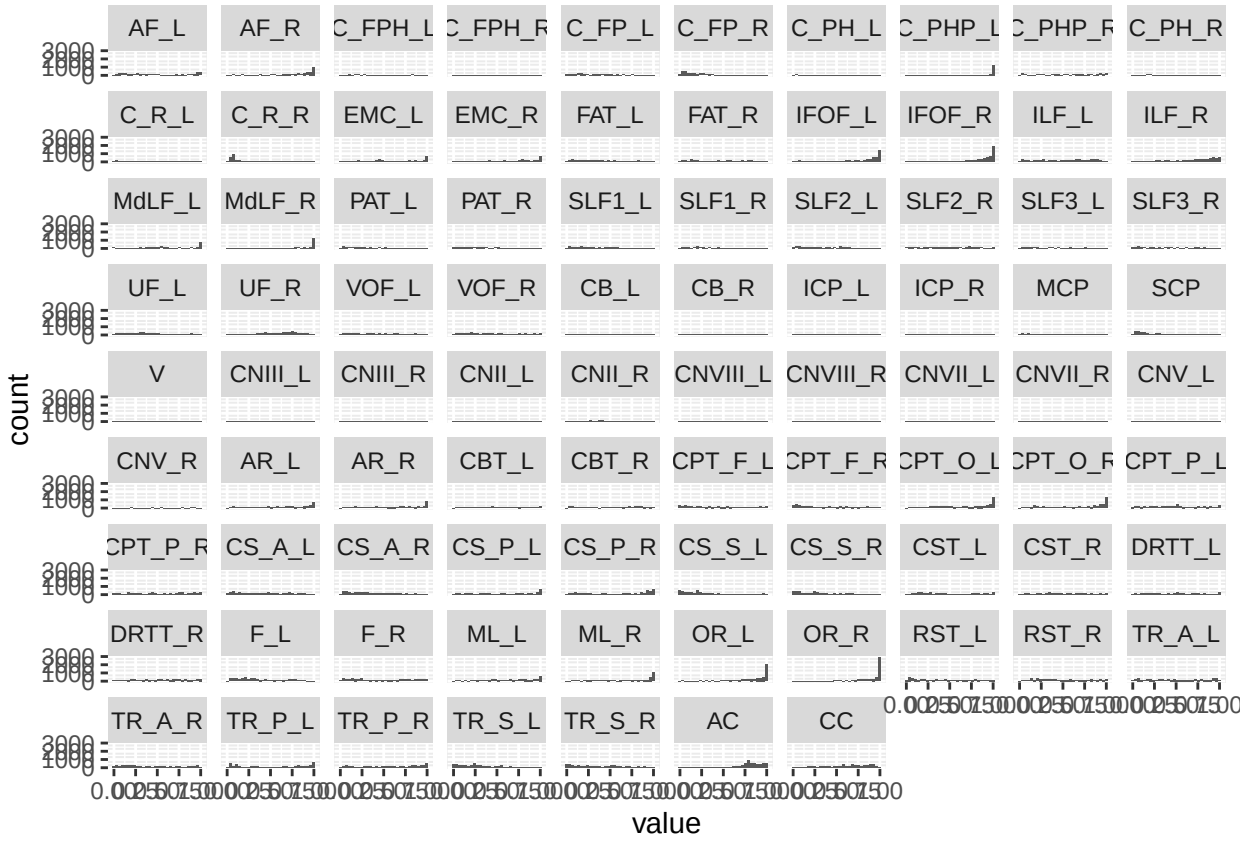

```
print(y)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```

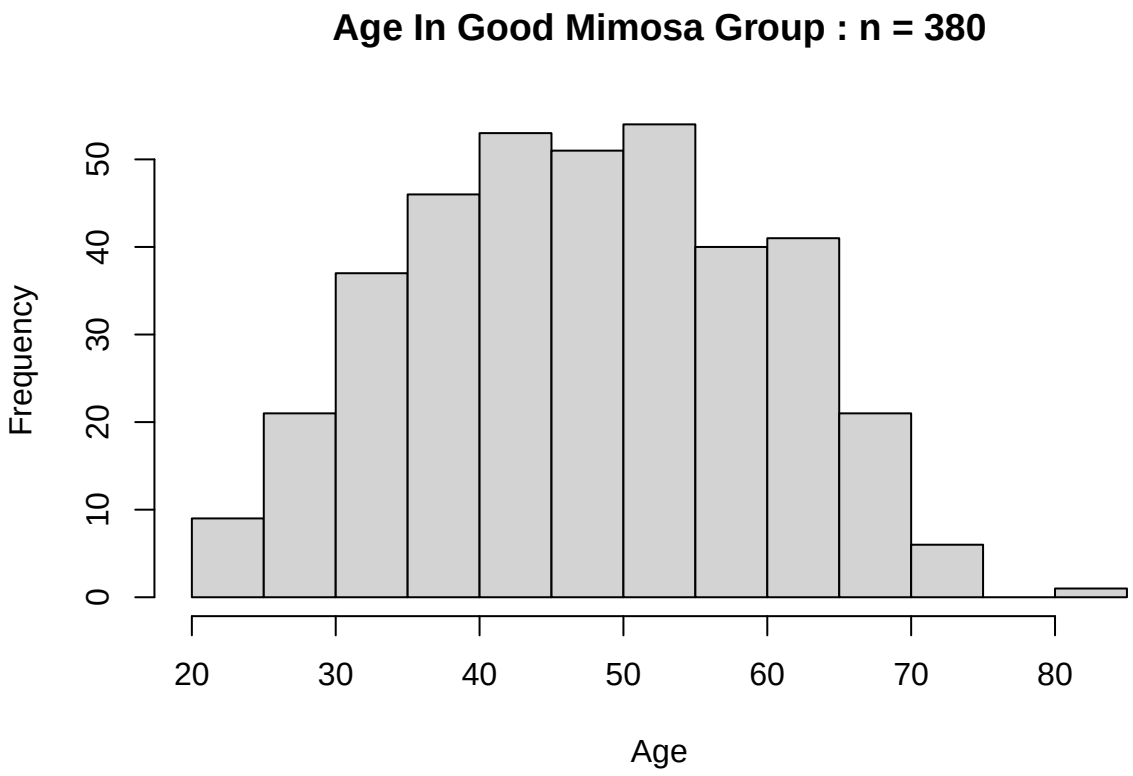



```
print(z)
```

```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```




```
############ age effect whole group

#isolate out only the depressed group and healthy group
dep_and_healthy_groups_for_ICD_analysis <- df_demo_and_fascicles %>%
  filter(depGroupVar != 0)  %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()


#### age histo ###
hist(dep_and_healthy_groups_for_ICD_analysis$PAT_AGE_AT_EXAM,
main = paste0("Age In Good Mimosa Group : n = ", dim(dep_and_healthy_groups_for_ICD_analysis)[1]), xlab
```




```
#lm
fascicle_age_lm <- lapply(fascicle_names, function(x)
{
  lm(substitute(i ~ PAT_AGE_AT_EXAM, list(i = as.name(x))), data = dep_and_healthy_groups_for_ICD_analys
})
names(fascicle_age_lm) <- fascicle_names

#anova
fascicle_age_anova <- lapply(fascicle_age_lm, anova)

#fdr corrected
fascicle_age_anova_fdr <- fdr_anova_generic(fascicle_age_anova, 1)
```

```
##              p_anova
## AF_L     1.310089e-04
## AF_R     6.949010e-03
## C_FPH_L  4.425597e-02
## C_FPH_R  9.013201e-01
## C_FP_L   1.057222e-02
## C_FP_R   1.756199e-01
## C_PH_L   6.944955e-01
## C_PHP_L  1.395585e-02
## C_PHP_R  4.952570e-03
## C_PH_R   2.931716e-02
## C_R_L    3.895358e-01
## C_R_R    6.220627e-01
```

```
## EMC_L    2.741087e-03
## EMC_R    5.201642e-03
## FAT_L    1.332697e-06
## FAT_R    5.112076e-08
## IFOF_L   1.173274e-05
## IFOF_R   5.828317e-04
## ILF_L    9.092300e-04
## ILF_R    3.065550e-02
## MdLF_L   4.787630e-03
## MdLF_R   1.678200e-01
## PAT_L    4.237933e-03
## PAT_R    2.143517e-03
## SLF1_L   3.090508e-03
## SLF1_R   1.115472e-01
## SLF2_L   3.981497e-04
## SLF2_R   3.517620e-05
## SLF3_L   5.209602e-06
## SLF3_R   1.705280e-08
## UF_L     2.819459e-06
## UF_R     1.393987e-09
## VOF_L    9.045875e-02
## VOF_R    2.545034e-03
## CB_L     1.736690e-01
## CB_R     5.141270e-01
## ICP_L    7.339899e-01
## ICP_R    1.499169e-01
## MCP      8.930558e-01
## SCP      2.278685e-03
## V        6.983386e-01
## CNIII_L  5.162906e-01
## CNIII_R  8.042341e-01
## CNII_L   9.535016e-01
## CNII_R   8.026877e-01
## CNVIII_L 6.294110e-01
## CNVIII_R 3.193122e-01
## CNVII_L  4.561844e-01
## CNVII_R  2.932914e-01
## CNV_L    2.622568e-01
## CNV_R    6.834446e-01
## AR_L     1.360755e-02
## AR_R     2.675391e-01
## CBT_L    9.296364e-04
## CBT_R    2.200882e-05
## CPT_F_L  1.690118e-05
## CPT_F_R  7.939947e-05
## CPT_O_L  1.106573e-03
## CPT_O_R  7.210236e-03
## CPT_P_L  1.856681e-02
## CPT_P_R  1.674531e-01
## CS_A_L   4.940336e-11
## CS_A_R   2.764136e-08
## CS_P_L   2.304313e-02
## CS_P_R   5.338406e-03
## CS_S_L   1.515914e-05
```

```
## CS_S_R   6.216574e-06
## CST_L    8.624774e-03
## CST_R    3.865901e-02
## DRTT_L   4.464285e-04
## DRTT_R   3.019916e-05
## F_L      3.589952e-01
## F_R      4.089012e-01
## ML_L     4.506021e-01
## ML_R     3.580214e-01
## OR_L     5.058345e-04
## OR_R     1.654767e-03
## RST_L    4.603385e-08
## RST_R    5.637520e-07
## TR_A_L   1.838190e-12
## TR_A_R   1.900999e-08
## TR_P_L   1.989410e-02
## TR_P_R   3.232031e-02
## TR_S_L   3.157539e-05
## TR_S_R   4.215605e-04
## AC       2.808699e-03
## CC       1.264964e-04
```

```
print(fascicle_age_anova_fdr)
```

```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.014
## 3     C_FP_L       0.02
## 4    C_PHP_L      0.025
## 5    C_PHP_R      0.011
## 6     C_PH_R      0.048
## 7      EMC_L      0.007
## 8      EMC_R      0.011
## 9      FAT_L          0
## 10     FAT_R          0
## 11    IFOF_L          0
## 12    IFOF_R      0.002
## 13     ILF_L      0.003
## 14     ILF_R      0.049
## 15    MdLF_L       0.01
## 16     PAT_L      0.009
## 17     PAT_R      0.006
## 18    SLF1_L      0.007
## 19    SLF2_L      0.001
## 20    SLF2_R          0
## 21    SLF3_L          0
## 22    SLF3_R          0
## 23      UF_L          0
## 24      UF_R          0
## 25     VOF_R      0.006
## 26       SCP      0.006
## 27      AR_L      0.025
## 28     CBT_L      0.003
## 29     CBT_R          0
```

```
## 30   CPT_F_L          0
## 31   CPT_F_R          0
## 32   CPT_O_L      0.003
## 33   CPT_O_R      0.014
## 34   CPT_P_L      0.032
## 35    CS_A_L          0
## 36    CS_A_R          0
## 37    CS_P_L      0.039
## 38    CS_P_R      0.011
## 39    CS_S_L          0
## 40    CS_S_R          0
## 41     CST_L      0.016
## 42    DRTT_L      0.001
## 43    DRTT_R          0
## 44      OR_L      0.002
## 45      OR_R      0.004
## 46     RST_L          0
## 47     RST_R          0
## 48    TR_A_L          0
## 49    TR_A_R          0
## 50    TR_P_L      0.034
## 51    TR_S_L          0
## 52    TR_S_R      0.001
## 53        AC      0.007
## 54        CC          0
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_age_anova[which(fascicle_bundle_mapping$name_vector == "asso
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##              p_anova
## AF_L    1.310089e-04
## AF_R    6.949010e-03
## C_FPH_L 4.425597e-02
## C_FPH_R 9.013201e-01
## C_FP_L  1.057222e-02
## C_FP_R  1.756199e-01
## C_PH_L  6.944955e-01
## C_PHP_L 1.395585e-02
## C_PHP_R 4.952570e-03
## C_PH_R  2.931716e-02
## C_R_L   3.895358e-01
## C_R_R   6.220627e-01
## EMC_L   2.741087e-03
## EMC_R   5.201642e-03
## FAT_L   1.332697e-06
## FAT_R   5.112076e-08
## IFOF_L  1.173274e-05
## IFOF_R  5.828317e-04
## ILF_L   9.092300e-04
## ILF_R   3.065550e-02
## MdLF_L  4.787630e-03
## MdLF_R  1.678200e-01
## PAT_L   4.237933e-03
```

```
## PAT_R   2.143517e-03
## SLF1_L  3.090508e-03
## SLF1_R  1.115472e-01
## SLF2_L  3.981497e-04
## SLF2_R  3.517620e-05
## SLF3_L  5.209602e-06
## SLF3_R  1.705280e-08
## UF_L    2.819459e-06
## UF_R    1.393987e-09
## VOF_L   9.045875e-02
## VOF_R   2.545034e-03
```

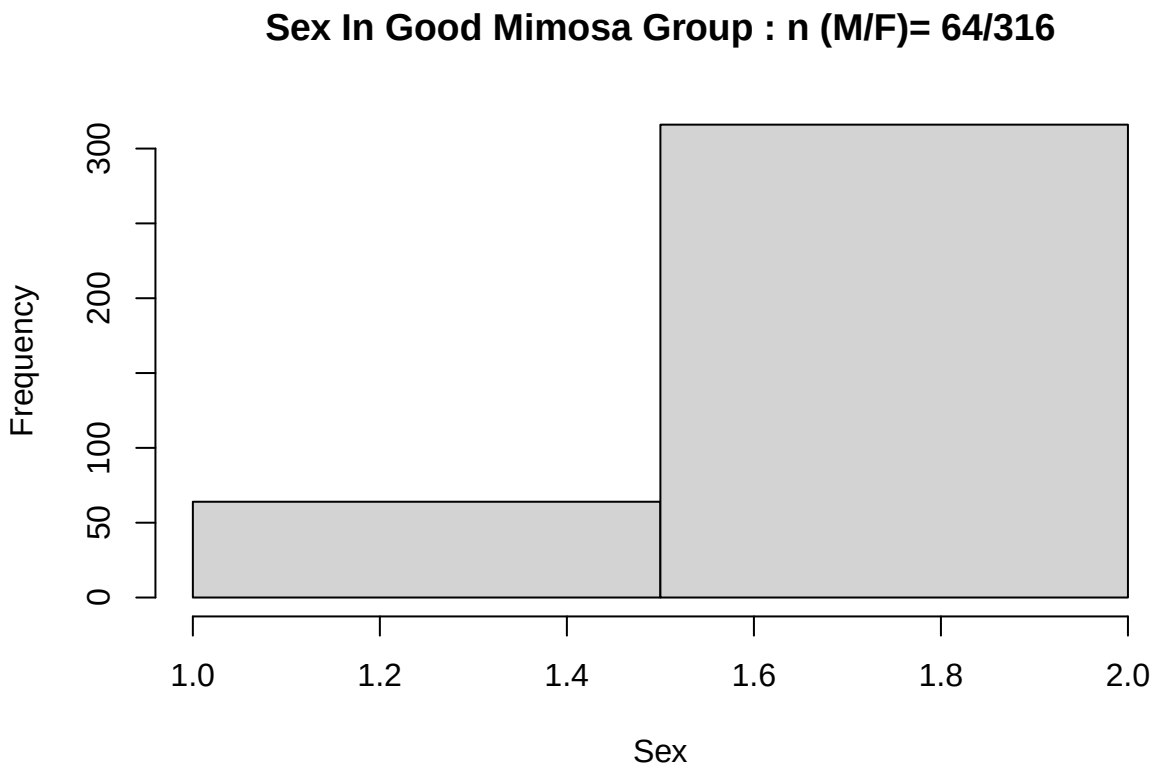
```
print(fascicle_anova_fdr_association)
```

```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.011
## 3     C_FP_L      0.016
## 4    C_PHP_L      0.021
## 5    C_PHP_R      0.009
## 6     C_PH_R      0.042
## 7      EMC_L      0.006
## 8      EMC_R      0.009
## 9      FAT_L          0
## 10     FAT_R          0
## 11    IFOF_L          0
## 12    IFOF_R      0.002
## 13     ILF_L      0.003
## 14     ILF_R      0.042
## 15    MdLF_L      0.009
## 16     PAT_L      0.008
## 17     PAT_R      0.006
## 18    SLF1_L      0.007
## 19    SLF2_L      0.001
## 20    SLF2_R          0
## 21    SLF3_L          0
## 22    SLF3_R          0
## 23      UF_L          0
## 24      UF_R          0
## 25     VOF_R      0.006
```

```
#visreg
#sapply(fascicle_age_lm,visreg)
```

```
### really not interesting at all. 3 areas that are uncorrected: SCP, CPT_O_R, OR_R

#isolate out only the depressed group and healthy group
dep_and_healthy_groups_for_ICD_analysis <- df_demo_and_fascicles %>% filter(depGroupVar != 0)  %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()
```

```
#### sex histo ###
hist(dep_and_healthy_groups_for_ICD_analysis$sex_binarized,
main = paste0("Sex In Good Mimosa Group : n (M/F)= ", sum(dep_and_healthy_groups_for_ICD_analysis$sex_b
```




```
#lm
fascicle_sex_lm <- lapply(fascicle_names, function(x)
{
  lm(substitute(i ~ osex, list(i = as.name(x))), data = dep_and_healthy_groups_for_ICD_analysis)
})
names(fascicle_sex_lm) <- fascicle_names

#anova
fascicle_sex_anova <- lapply(fascicle_sex_lm, anova)

#fdr corrected
fascicle_sex_anova_fdr <- fdr_anova_generic(fascicle_sex_anova, 1)
```

```
##            p_anova
## AF_L     0.44739266
## AF_R     0.64416738
## C_FPH_L  0.94437159
## C_FPH_R  0.53001016
## C_FP_L   0.48158913
## C_FP_R   0.80476904
## C_PH_L   0.61020308
```

```
## C_PHP_L  0.67545646
## C_PHP_R  0.07801124
## C_PH_R   0.10468261
## C_R_L    0.69227951
## C_R_R    0.98937394
## EMC_L    0.65989277
## EMC_R    0.82951422
## FAT_L    0.50035207
## FAT_R    0.77136690
## IFOF_L   0.92843465
## IFOF_R   0.23656430
## ILF_L    0.91105639
## ILF_R    0.30099126
## MdLF_L   0.77788757
## MdLF_R   0.78066200
## PAT_L    0.86985177
## PAT_R    0.57869897
## SLF1_L   0.65107626
## SLF1_R   0.42036259
## SLF2_L   0.36090055
## SLF2_R   0.97316633
## SLF3_L   0.38815774
## SLF3_R   0.50987210
## UF_L     0.95985961
## UF_R     0.93716889
## VOF_L    0.38583828
## VOF_R    0.95224203
## CB_L     0.63783304
## CB_R     0.76441140
## ICP_L    0.77509495
## ICP_R    0.18945834
## MCP      0.32136336
## SCP      0.03673865
## V        0.94298106
## CNIII_L  0.23441378
## CNIII_R  0.48458154
## CNII_L   0.62881790
## CNII_R   0.85684474
## CNVIII_L 0.79168064
## CNVIII_R 0.05493746
## CNVII_L  0.98462390
## CNVII_R  0.60142671
## CNV_L    0.66516260
## CNV_R    0.50351688
## AR_L     0.83663191
## AR_R     0.51185386
## CBT_L    0.68128856
## CBT_R    0.65052661
## CPT_F_L  0.57224667
## CPT_F_R  0.29541661
## CPT_O_L  0.49017750
## CPT_O_R  0.03375782
## CPT_P_L  0.36175528
## CPT_P_R  0.29446565
```

```
## CS_A_L   0.99428287
## CS_A_R   0.70794107
## CS_P_L   0.80484116
## CS_P_R   0.23435091
## CS_S_L   0.55385787
## CS_S_R   0.59913677
## CST_L    0.10465867
## CST_R    0.21079679
## DRTT_L   0.16582914
## DRTT_R   0.11019961
## F_L      0.15411012
## F_R      0.67638975
## ML_L     0.37068476
## ML_R     0.35207309
## OR_L     0.34692466
## OR_R     0.03134048
## RST_L    0.58358562
## RST_R    0.82993497
## TR_A_L   0.87865704
## TR_A_R   0.79047829
## TR_P_L   0.50045358
## TR_P_R   0.53155061
## TR_S_L   0.58894961
## TR_S_R   0.62770144
## AC       0.22363790
## CC       0.32643168
```

```
print(fascicle_sex_anova_fdr)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_sex_anova[which(fascicle_bundle_mapping$name_vector == "asso
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.44739266
## AF_R    0.64416738
## C_FPH_L 0.94437159
## C_FPH_R 0.53001016
## C_FP_L  0.48158913
## C_FP_R  0.80476904
## C_PH_L  0.61020308
## C_PHP_L 0.67545646
## C_PHP_R 0.07801124
## C_PH_R  0.10468261
## C_R_L   0.69227951
## C_R_R   0.98937394
## EMC_L   0.65989277
## EMC_R   0.82951422
## FAT_L   0.50035207
## FAT_R   0.77136690
```

```
## IFOF_L  0.92843465
## IFOF_R  0.23656430
## ILF_L   0.91105639
## ILF_R   0.30099126
## MdLF_L  0.77788757
## MdLF_R  0.78066200
## PAT_L   0.86985177
## PAT_R   0.57869897
## SLF1_L  0.65107626
## SLF1_R  0.42036259
## SLF2_L  0.36090055
## SLF2_R  0.97316633
## SLF3_L  0.38815774
## SLF3_R  0.50987210
## UF_L    0.95985961
## UF_R    0.93716889
## VOF_L   0.38583828
## VOF_R   0.95224203
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_sex_anova[which(fascicle_bundle_mapping$inDepNetwork_vector 1
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.44739266
## AF_R    0.64416738
## C_PHP_R 0.07801124
## EMC_L   0.65989277
## EMC_R   0.82951422
## FAT_L   0.50035207
## FAT_R   0.77136690
## IFOF_L  0.92843465
## IFOF_R  0.23656430
## ILF_R   0.30099126
## MdLF_L  0.77788757
## MdLF_R  0.78066200
## PAT_L   0.86985177
## PAT_R   0.57869897
## SLF2_L  0.36090055
## SLF2_R  0.97316633
## SLF3_L  0.38815774
## SLF3_R  0.50987210
## V       0.94298106
## AR_R    0.51185386
## CBT_L   0.68128856
## CBT_R   0.65052661
## CPT_F_L 0.57224667
## CPT_F_R 0.29541661
```

```
## CPT_O_L 0.49017750
## CPT_O_R 0.03375782
## CPT_P_L 0.36175528
## CPT_P_R 0.29446565
## CS_A_L  0.99428287
## CS_A_R  0.70794107
## CS_P_L  0.80484116
## CS_P_R  0.23435091
## CS_S_L  0.55385787
## CS_S_R  0.59913677
## CST_L   0.10465867
## CST_R   0.21079679
## DRTT_R  0.11019961
## ML_L    0.37068476
## RST_L   0.58358562
## RST_R   0.82993497
## TR_A_L  0.87865704
## TR_A_R  0.79047829
## TR_P_L  0.50045358
## TR_P_R  0.53155061
## TR_S_L  0.58894961
## TR_S_R  0.62770144
## CC      0.32643168
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#uncorrected
fascicle_sex_anova_p <- sapply(fascicle_sex_anova, function(v) v$"Pr(>F)"[1])
fascicle_sex_anova_p05_unc <- as.data.frame(fascicle_sex_anova_p[fascicle_sex_anova_p < 0.05])
print(fascicle_sex_anova_p05_unc)
```

```
##         fascicle_sex_anova_p[fascicle_sex_anova_p < 0.05]
## SCP                                            0.03673865
## CPT_O_R                                        0.03375782
## OR_R                                           0.03134048
```

```
#isolate out only the depressed group and healthy group, make a column that sums up the total prop lost
dep_and_healthy_groups_for_ICD_analysis <- df_demo_and_fascicles %>%
  filter(depGroupVar != 0)  %>%
  mutate(total_fascicle_prop_lost = rowMeans(across(fascicle_names))) %>%
  mutate(total_fascicle_prop_lost_indepnet = rowMeans(across(fascicle_names_dep_network_all))) %>%
  mutate(total_fascicle_prop_lost_indepnet_10_percent =
           rowMeans(across(fascicle_names_dep_network_10_percent))) %>%
  mutate(total_fascicle_prop_lost_nondep_network =
           rowMeans(across(fascicle_names_nondep_network))) %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()
```

```
## Note: Using an external vector in selections is ambiguous.
## i Use ‘all_of(fascicle_names)‘ instead of ‘fascicle_names‘ to silence this message.
## i See <https://tidyselect.r-lib.org/reference/faq-external-vector.html>.
## This message is displayed once per session.


## Note: Using an external vector in selections is ambiguous.
## i Use ‘all_of(fascicle_names_dep_network_all)‘ instead of ‘fascicle_names_dep_network_all‘ to silenc
## i See <https://tidyselect.r-lib.org/reference/faq-external-vector.html>.
## This message is displayed once per session.


## Note: Using an external vector in selections is ambiguous.
## i Use ‘all_of(fascicle_names_dep_network_10_percent)‘ instead of ‘fascicle_names_dep_network_10_perc
## i See <https://tidyselect.r-lib.org/reference/faq-external-vector.html>.
## This message is displayed once per session.


## Note: Using an external vector in selections is ambiguous.
## i Use ‘all_of(fascicle_names_nondep_network)‘ instead of ‘fascicle_names_nondep_network‘ to silence
## i See <https://tidyselect.r-lib.org/reference/faq-external-vector.html>.
## This message is displayed once per session.
```

```
dep_vs_healthy <- lm(total_fascicle_prop_lost ~ depGroupVar, data = dep_and_healthy_groups_for_ICD_anal
summary(dep_vs_healthy) #p=0.494
```

```
##
## Call:
## lm(formula = total_fascicle_prop_lost ~ depGroupVar, data = dep_and_healthy_groups_for_ICD_analysis)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.27380 -0.14621 -0.03435  0.10915  0.45452
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.19970    0.03162   6.316 7.54e-10 ***
## depGroupVar  0.03705    0.01879   1.972   0.0494 *
## ---
## Signif. codes:  0 ’***’ 0.001 ’**’ 0.01 ’*’ 0.05 ’.’ 0.1 ’ ’ 1
##
## Residual standard error: 0.1786 on 378 degrees of freedom
## Multiple R-squared:  0.01018,    Adjusted R-squared:  0.007561
## F-statistic: 3.887 on 1 and 378 DF,  p-value: 0.04938
```

```
#test whether proportion lost overall different between depressed and healthy- yes, p = 0.049
total_volume_lost_dep_vs_healthy_unique <- t.test(dep_and_healthy_groups_for_ICD_analysis$total_fascicl

#look at within depression network specifically - trend, p = 0.059
total_volume_lost_dep_vs_healthy_unique_in_dep_network <- t.test(dep_and_healthy_groups_for_ICD_analysi

#look at within depression network in fascicles where at least 10% of the volume of the fascicle was in
#yes, p = 0.048
total_volume_lost_dep_vs_healthy_unique_in_dep_network_10percent <- t.test(dep_and_healthy_groups_for_I
```

```r
#look at outside depression network, yes p = 0.037
total_volume_lost_dep_vs_healthy_unique_in_nondep_network <- t.test(dep_and_healthy_groups_for_ICD_analy

### Age actually makes things worse
#dep_vs_healthy_w_age <- lm(total_fascicle_prop_lost ~ depGroupVar + PAT_AGE_AT_EXAM, data = dep_and_he
#summary(dep_vs_healthy_w_age)
```

```r
##### repeat above analysis but use only the first instance of each EMPI, sorted by date
df_unique_empi <- df_demo_and_fascicles %>%
  filter(depGroupVar != 0) %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ungroup()


#lm
fascicle_lm_unique <- lapply(fascicle_names, function(x)
{
  lm(substitute(i ~ depGroupVar + PAT_AGE_AT_EXAM, list(i = as.name(x))), data = df_unique_empi)
})
names(fascicle_lm_unique) <- fascicle_names

#anova
fascicle_anova_unique <- lapply(fascicle_lm_unique, anova)

#fdr corrected
fascicle_anova_unique_fdr <- fdr_anova_generic(fascicle_anova_unique, 1)
```

```
##             p_anova
## AF_L     0.06407845
## AF_R     0.01168289
## C_FPH_L  0.32605588
## C_FPH_R  0.47509569
## C_FP_L   0.27111149
## C_FP_R   0.97152132
## C_PH_L   0.17926341
## C_PHP_L  0.35242463
## C_PHP_R  0.61825578
## C_PH_R   0.67565811
## C_R_L    0.24158191
## C_R_R    0.45306430
## EMC_L    0.59912011
## EMC_R    0.38875691
## FAT_L    0.14914559
## FAT_R    0.01828607
## IFOF_L   0.24875100
## IFOF_R   0.12279240
## ILF_L    0.14886559
## ILF_R    0.06810370
## MdLF_L   0.28461980
## MdLF_R   0.33672238
## PAT_L    0.44607396
```

```
## PAT_R    0.10881473
## SLF1_L   0.11079249
## SLF1_R   0.09157192
## SLF2_L   0.35889244
## SLF2_R   0.01901378
## SLF3_L   0.78826391
## SLF3_R   0.06138941
## UF_L     0.53145734
## UF_R     0.29585849
## VOF_L    0.80123032
## VOF_R    0.04741569
## CB_L     0.64962368
## CB_R     0.49703868
## ICP_L    0.66332943
## ICP_R    0.07945415
## MCP      0.74188711
## SCP      0.34158578
## V        0.33067565
## CNIII_L  0.77775279
## CNIII_R  0.78348359
## CNII_L   0.15253697
## CNII_R   0.69024050
## CNVIII_L 0.28793387
## CNVIII_R 0.53043822
## CNVII_L  0.34443485
## CNVII_R  0.57400949
## CNV_L    0.26800388
## CNV_R    0.48294092
## AR_L     0.13161434
## AR_R     0.13952963
## CBT_L    0.09569982
## CBT_R    0.09943900
## CPT_F_L  0.09796600
## CPT_F_R  0.02887163
## CPT_O_L  0.02238344
## CPT_O_R  0.08224713
## CPT_P_L  0.27315089
## CPT_P_R  0.02053104
## CS_A_L   0.40732659
## CS_A_R   0.17325955
## CS_P_L   0.20672426
## CS_P_R   0.19153174
## CS_S_L   0.10197510
## CS_S_R   0.03783654
## CST_L    0.14022819
## CST_R    0.07674057
## DRTT_L   0.05173042
## DRTT_R   0.00695066
## F_L      0.11572312
## F_R      0.18192398
## ML_L     0.36178444
## ML_R     0.02511932
## OR_L     0.14198585
## OR_R     0.07106503
```

```
## RST_L    0.36041798
## RST_R    0.13416577
## TR_A_L   0.34011449
## TR_A_R   0.04140249
## TR_P_L   0.10396597
## TR_P_R   0.03952872
## TR_S_L   0.13366584
## TR_S_R   0.01067045
## AC       0.09987928
## CC       0.05198533
```

```
print(fascicle_anova_unique_fdr)#anova values < 0.05, uncorrected
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_anova_unique[which(fascicle_bundle_mapping$name_vector == "as
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.06407845
## AF_R    0.01168289
## C_FPH_L 0.32605588
## C_FPH_R 0.47509569
## C_FP_L  0.27111149
## C_FP_R  0.97152132
## C_PH_L  0.17926341
## C_PHP_L 0.35242463
## C_PHP_R 0.61825578
## C_PH_R  0.67565811
## C_R_L   0.24158191
## C_R_R   0.45306430
## EMC_L   0.59912011
## EMC_R   0.38875691
## FAT_L   0.14914559
## FAT_R   0.01828607
## IFOF_L  0.24875100
## IFOF_R  0.12279240
## ILF_L   0.14886559
## ILF_R   0.06810370
## MdLF_L  0.28461980
## MdLF_R  0.33672238
## PAT_L   0.44607396
## PAT_R   0.10881473
## SLF1_L  0.11079249
## SLF1_R  0.09157192
## SLF2_L  0.35889244
## SLF2_R  0.01901378
## SLF3_L  0.78826391
## SLF3_R  0.06138941
## UF_L    0.53145734
## UF_R    0.29585849
```

```
## VOF_L   0.80123032
## VOF_R   0.04741569
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only dep network
fascicle_anova_w_fiber_mapping <- fascicle_anova_unique[which(fascicle_bundle_mapping$inDepNetwork_vecto
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.06407845
## AF_R    0.01168289
## C_PHP_R 0.61825578
## EMC_L   0.59912011
## EMC_R   0.38875691
## FAT_L   0.14914559
## FAT_R   0.01828607
## IFOF_L  0.24875100
## IFOF_R  0.12279240
## ILF_R   0.06810370
## MdLF_L  0.28461980
## MdLF_R  0.33672238
## PAT_L   0.44607396
## PAT_R   0.10881473
## SLF2_L  0.35889244
## SLF2_R  0.01901378
## SLF3_L  0.78826391
## SLF3_R  0.06138941
## V       0.33067565
## AR_R    0.13952963
## CBT_L   0.09569982
## CBT_R   0.09943900
## CPT_F_L 0.09796600
## CPT_F_R 0.02887163
## CPT_O_L 0.02238344
## CPT_O_R 0.08224713
## CPT_P_L 0.27315089
## CPT_P_R 0.02053104
## CS_A_L  0.40732659
## CS_A_R  0.17325955
## CS_P_L  0.20672426
## CS_P_R  0.19153174
## CS_S_L  0.10197510
## CS_S_R  0.03783654
## CST_L   0.14022819
## CST_R   0.07674057
## DRTT_R  0.00695066
## ML_L    0.36178444
## RST_L   0.36041798
## RST_R   0.13416577
```

```
## TR_A_L  0.34011449
## TR_A_R  0.04140249
## TR_P_L  0.10396597
## TR_P_R  0.03952872
## TR_S_L  0.13366584
## TR_S_R  0.01067045
## CC      0.05198533
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only dep 10% mask
fascicle_anova_w_fiber_mapping <- fascicle_anova_unique[which(fascicle_bundle_mapping$inDepNetwork_vecto
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.06407845
## AF_R    0.01168289
## C_PHP_R 0.61825578
## FAT_L   0.14914559
## FAT_R   0.01828607
## MdLF_L  0.28461980
## MdLF_R  0.33672238
## SLF2_L  0.35889244
## SLF2_R  0.01901378
## SLF3_R  0.06138941
## CBT_L   0.09569982
## CBT_R   0.09943900
## CPT_O_R 0.08224713
## CS_P_R  0.19153174
## TR_P_R  0.03952872
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#uncorrected
fascicle_anova_unique_p <- sapply(fascicle_anova_unique, function(v) v$"Pr(>F)"[1])
fascicle_anova_unique_p05_unc <- as.data.frame(fascicle_anova_unique_p[fascicle_anova_unique_p < 0.05])
print(fascicle_anova_unique_p05_unc)
```

```
##         fascicle_anova_unique_p[fascicle_anova_unique_p < 0.05]
## AF_R                                                 0.01168289
## FAT_R                                                0.01828607
## SLF2_R                                               0.01901378
## VOF_R                                                0.04741569
## CPT_F_R                                              0.02887163
## CPT_O_L                                              0.02238344
```

```
## CPT_P_R                                                0.02053104
## CS_S_R                                                 0.03783654
## DRTT_R                                                 0.00695066
## ML_R                                                   0.02511932
## TR_A_R                                                 0.04140249
## TR_P_R                                                 0.03952872
## TR_S_R                                                 0.01067045
```

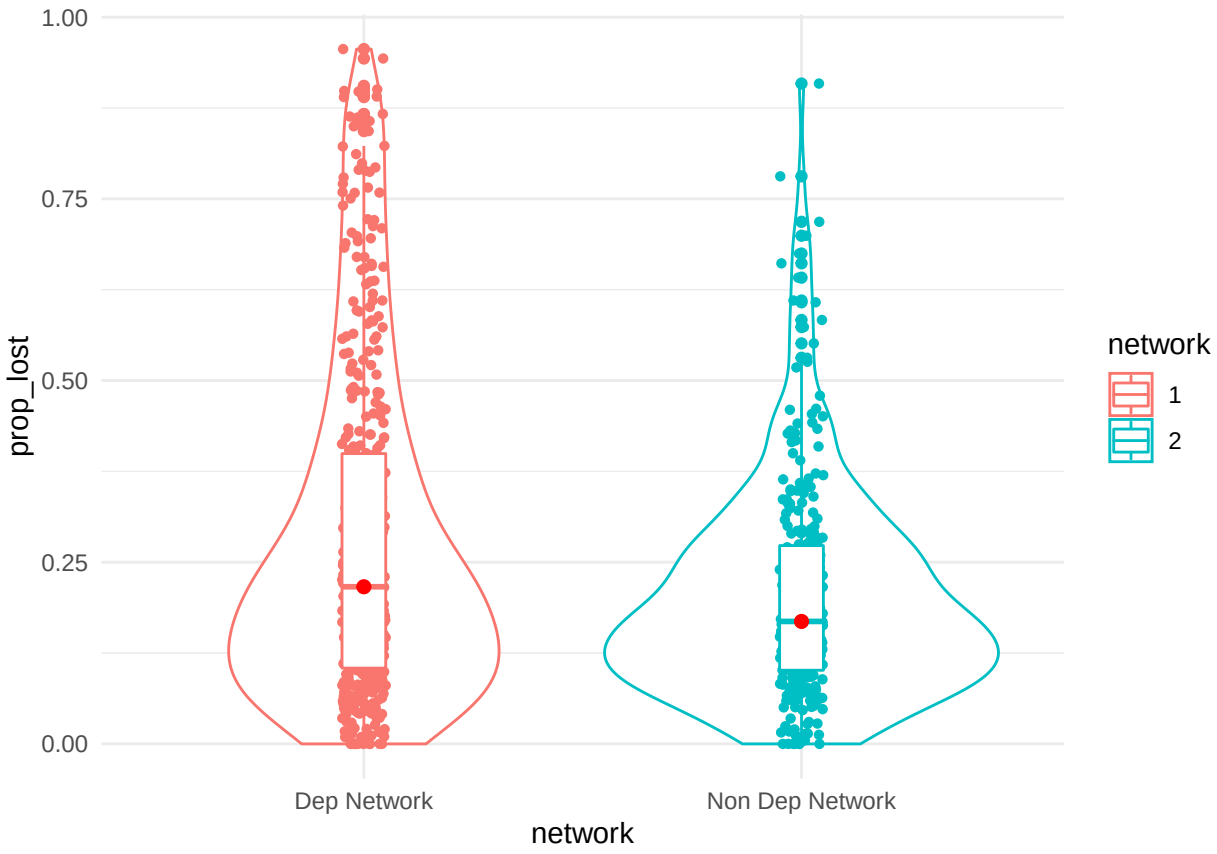
```
### tests whether there is higher proportion of vertices lost in depression network versus not

dep_and_healthy_groups_for_ICD_analysis <- df_demo_and_fascicles %>%
  filter(depGroupVar != 0)  %>%
  mutate(total_fascicle_prop_lost = rowMeans(across(fascicle_names))) %>%
  mutate(total_fascicle_prop_lost_indepnet = rowMeans(across(fascicle_names_dep_network_all))) %>%
  mutate(total_fascicle_prop_lost_indepnet_10_percent =
           rowMeans(across(fascicle_names_dep_network_10_percent))) %>%
  mutate(total_fascicle_prop_lost_nondep_network =
           rowMeans(across(fascicle_names_nondep_network))) %>%
  group_by(EMPI) %>%
  arrange(EXAM_DATE) %>%
  slice(1) %>%
  ### when I filter and remove fascicles where there was no loss at all, the depression vs healthy findi
#  filter(total_fascicle_prop_lost > 0) %>%
  ungroup()


#test whether there is differentially more volume loss in depression versus nondepression network
volume_lost_dep_vs_nondep_network_unique <- t.test(dep_and_healthy_groups_for_ICD_analysis$total_fascicl

volume_lost_dep10_vs_nondep_network_unique <- t.test(dep_and_healthy_groups_for_ICD_analysis$total_fasci
dep_and_healthy_groups_for_ICD_analysis$total_fascicle_prop_lost_nondep_network, var.equal = F) #mean d


#df for visreg - actually not using visreg. Just a nice way to see that there is significantly more los
df_for_visreg <- as.data.frame(cbind(c(dep_and_healthy_groups_for_ICD_analysis$EMPI, dep_and_healthy_gr
```

```
## Warning in cbind(c(dep_and_healthy_groups_for_ICD_analysis$EMPI,
## dep_and_healthy_groups_for_ICD_analysis$EMPI), : number of rows of result is not
## a multiple of vector length (arg 3)
```

```
names(df_for_visreg) <- c("EMPI", "prop_lost", "network")
df_for_visreg$network <- as.factor(df_for_visreg$network)

plot <- ggplot(df_for_visreg, aes(x=network, y = prop_lost, col=network)) +
  geom_violin() +
  geom_jitter(shape=16, position=position_jitter(0.05)) +
  geom_boxplot(width=0.1) + theme_minimal() +
  stat_summary(fun.y=median, geom="point", size=2, color="red") +
  scale_x_discrete(labels=c("1" = "Dep Network", "2" = "Non Dep Network"))
```

```
## Warning: `fun.y` is deprecated. Use `fun` instead.
```

```
print(plot)
```




```
###### Depression network x depression group interaction - It is there, depression always worse.
#these lms largely match up with the t.tests above. Sig differences between depressed (more disease) wi

loss_in_dep_network <- lm(total_fascicle_prop_lost_indepnet~depGroupVar, data = dep_and_healthy_groups_
loss_in_dep_network_10_percent <- lm(total_fascicle_prop_lost_indepnet_10_percent~depGroupVar, data = d
loss_in_nondep_network <- lm(total_fascicle_prop_lost_nondep_network~depGroupVar, data = dep_and_healthy
```

All the mixed models are below

```
### This subscript compares proportion of fascicles lost across age for each fascicle of the 80+. Looks
### Separately considers findings just within the association cortex

#isolate out only the depressed group and healthy group
df_mm <- df_demo_and_fascicles %>% filter(depGroupVar != 0)
#n depressed = 859, healthy = 604, total n = 1463


#lm
fascicle_lm_mm <- lapply(fascicle_names, function(x)
{
  lmerTest::lmer(substitute(i ~ PAT_AGE_AT_EXAM + (1 | EMPI), list(i = as.name(x))), data = df_mm)
})
names(fascicle_lm_mm) <- fascicle_names
```

```r
#anova
fascicle_anova_mm <- lapply(fascicle_lm_mm, anova)

#fdr corrected
fascicle_anova_mm_fdr <- fdr_anova_generic(fascicle_anova_mm, 1)
```

```
##                p_anova
## AF_L     1.091485e-05
## AF_R     2.467021e-03
## C_FPH_L  4.984001e-02
## C_FPH_R  5.627960e-01
## C_FP_L   3.886481e-03
## C_FP_R   1.644328e-01
## C_PH_L   5.090131e-01
## C_PHP_L  1.181989e-02
## C_PHP_R  8.534313e-03
## C_PH_R   3.252155e-02
## C_R_L    5.661203e-02
## C_R_R    1.748032e-01
## EMC_L    1.001833e-02
## EMC_R    8.104994e-03
## FAT_L    3.504740e-09
## FAT_R    1.151864e-08
## IFOF_L   2.634713e-04
## IFOF_R   1.480628e-02
## ILF_L    5.165942e-03
## ILF_R    1.613273e-01
## MdLF_L   6.225199e-03
## MdLF_R   4.272190e-01
## PAT_L    1.514194e-02
## PAT_R    2.515301e-03
## SLF1_L   4.848380e-03
## SLF1_R   8.784166e-02
## SLF2_L   1.118391e-04
## SLF2_R   5.330751e-06
## SLF3_L   2.013766e-06
## SLF3_R   2.709435e-07
## UF_L     3.839107e-06
## UF_R     2.625400e-09
## VOF_L    1.043608e-01
## VOF_R    7.899826e-03
## CB_L     2.236696e-01
## CB_R     5.254563e-01
## ICP_L    9.439088e-01
## ICP_R    2.016259e-01
## MCP      8.473377e-01
## SCP      6.243069e-04
## V        4.206295e-01
## CNIII_L  5.706282e-01
## CNIII_R  7.016977e-01
## CNII_L   8.927607e-01
## CNII_R   4.230851e-01
## CNVIII_L 4.019360e-01
```

```
## CNVIII_R 3.580092e-01
## CNVII_L  1.068039e-01
## CNVII_R  2.418218e-01
## CNV_L    1.627774e-01
## CNV_R    9.224495e-01
## AR_L     2.138359e-02
## AR_R     2.117593e-01
## CBT_L    1.905821e-03
## CBT_R    1.529588e-06
## CPT_F_L  1.291364e-07
## CPT_F_R  9.554555e-06
## CPT_O_L  3.610910e-03
## CPT_O_R  5.241754e-03
## CPT_P_L  1.335207e-01
## CPT_P_R  1.283468e-01
## CS_A_L   2.403762e-11
## CS_A_R   5.743437e-08
## CS_P_L   5.186277e-02
## CS_P_R   4.292888e-03
## CS_S_L   2.739498e-06
## CS_S_R   2.356204e-06
## CST_L    1.065456e-02
## CST_R    1.748282e-02
## DRTT_L   2.438658e-05
## DRTT_R   8.061692e-06
## F_L      2.617095e-01
## F_R      3.995970e-01
## ML_L     6.500090e-01
## ML_R     2.101848e-01
## OR_L     2.633757e-03
## OR_R     1.854511e-02
## RST_L    6.118111e-09
## RST_R    4.270105e-08
## TR_A_L   3.314413e-12
## TR_A_R   2.332114e-08
## TR_P_L   2.192477e-02
## TR_P_R   3.710924e-02
## TR_S_L   4.302964e-06
## TR_S_R   1.651505e-04
## AC       1.706126e-02
## CC       4.716604e-04
```

```
print(fascicle_anova_mm_fdr)#anova values < 0.05, uncorrected
```

```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.007
## 3     C_FP_L       0.01
## 4    C_PHP_L      0.023
## 5    C_PHP_R      0.018
## 6      EMC_L      0.021
## 7      EMC_R      0.018
## 8      FAT_L          0
## 9      FAT_R          0
```

```
## 10    IFOF_L      0.001
## 11    IFOF_R      0.029
## 12     ILF_L      0.012
## 13    MdLF_L      0.014
## 14     PAT_L      0.029
## 15     PAT_R      0.007
## 16    SLF1_L      0.012
## 17    SLF2_L          0
## 18    SLF2_R          0
## 19    SLF3_L          0
## 20    SLF3_R          0
## 21      UF_L          0
## 22      UF_R          0
## 23     VOF_R      0.018
## 24       SCP      0.002
## 25      AR_L      0.037
## 26     CBT_L      0.006
## 27     CBT_R          0
## 28   CPT_F_L          0
## 29   CPT_F_R          0
## 30   CPT_O_L       0.01
## 31   CPT_O_R      0.012
## 32    CS_A_L          0
## 33    CS_A_R          0
## 34    CS_P_R      0.011
## 35    CS_S_L          0
## 36    CS_S_R          0
## 37     CST_L      0.022
## 38     CST_R      0.032
## 39    DRTT_L          0
## 40    DRTT_R          0
## 41      OR_L      0.007
## 42      OR_R      0.033
## 43     RST_L          0
## 44     RST_R          0
## 45    TR_A_L          0
## 46    TR_A_R          0
## 47    TR_P_L      0.037
## 48    TR_S_L          0
## 49    TR_S_R      0.001
## 50        AC      0.032
## 51        CC      0.002
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$name_vector == "assoc
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##              p_anova
## AF_L    1.091485e-05
## AF_R    2.467021e-03
## C_FPH_L 4.984001e-02
## C_FPH_R 5.627960e-01
## C_FP_L  3.886481e-03
## C_FP_R  1.644328e-01
```

```
## C_PH_L  5.090131e-01
## C_PHP_L 1.181989e-02
## C_PHP_R 8.534313e-03
## C_PH_R  3.252155e-02
## C_R_L   5.661203e-02
## C_R_R   1.748032e-01
## EMC_L   1.001833e-02
## EMC_R   8.104994e-03
## FAT_L   3.504740e-09
## FAT_R   1.151864e-08
## IFOF_L  2.634713e-04
## IFOF_R  1.480628e-02
## ILF_L   5.165942e-03
## ILF_R   1.613273e-01
## MdLF_L  6.225199e-03
## MdLF_R  4.272190e-01
## PAT_L   1.514194e-02
## PAT_R   2.515301e-03
## SLF1_L  4.848380e-03
## SLF1_R  8.784166e-02
## SLF2_L  1.118391e-04
## SLF2_R  5.330751e-06
## SLF3_L  2.013766e-06
## SLF3_R  2.709435e-07
## UF_L    3.839107e-06
## UF_R    2.625400e-09
## VOF_L   1.043608e-01
## VOF_R   7.899826e-03
```

```
print(fascicle_anova_fdr_association)
```

```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.007
## 3     C_FP_L       0.01
## 4    C_PHP_L      0.019
## 5    C_PHP_R      0.015
## 6     C_PH_R      0.046
## 7      EMC_L      0.017
## 8      EMC_R      0.015
## 9      FAT_L          0
## 10     FAT_R          0
## 11    IFOF_L      0.001
## 12    IFOF_R      0.022
## 13     ILF_L      0.012
## 14    MdLF_L      0.013
## 15     PAT_L      0.022
## 16     PAT_R      0.007
## 17    SLF1_L      0.012
## 18    SLF2_L          0
## 19    SLF2_R          0
## 20    SLF3_L          0
## 21    SLF3_R          0
## 22      UF_L          0
```

```
## 23      UF_R          0
## 24     VOF_R      0.015
```

```
#fdr corrected only dep network
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$inDepNetwork_vector >(
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##              p_anova
## AF_L    1.091485e-05
## AF_R    2.467021e-03
## C_PHP_R 8.534313e-03
## EMC_L   1.001833e-02
## EMC_R   8.104994e-03
## FAT_L   3.504740e-09
## FAT_R   1.151864e-08
## IFOF_L  2.634713e-04
## IFOF_R  1.480628e-02
## ILF_R   1.613273e-01
## MdLF_L  6.225199e-03
## MdLF_R  4.272190e-01
## PAT_L   1.514194e-02
## PAT_R   2.515301e-03
## SLF2_L  1.118391e-04
## SLF2_R  5.330751e-06
## SLF3_L  2.013766e-06
## SLF3_R  2.709435e-07
## V       4.206295e-01
## AR_R    2.117593e-01
## CBT_L   1.905821e-03
## CBT_R   1.529588e-06
## CPT_F_L 1.291364e-07
## CPT_F_R 9.554555e-06
## CPT_O_L 3.610910e-03
## CPT_O_R 5.241754e-03
## CPT_P_L 1.335207e-01
## CPT_P_R 1.283468e-01
## CS_A_L  2.403762e-11
## CS_A_R  5.743437e-08
## CS_P_L  5.186277e-02
## CS_P_R  4.292888e-03
## CS_S_L  2.739498e-06
## CS_S_R  2.356204e-06
## CST_L   1.065456e-02
## CST_R   1.748282e-02
## DRTT_R  8.061692e-06
## ML_L    6.500090e-01
## RST_L   6.118111e-09
## RST_R   4.270105e-08
## TR_A_L  3.314413e-12
## TR_A_R  2.332114e-08
## TR_P_L  2.192477e-02
## TR_P_R  3.710924e-02
## TR_S_L  4.302964e-06
## TR_S_R  1.651505e-04
```

```
## CC      4.716604e-04
```

```
print(fascicle_anova_fdr_association)
```

```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.005
## 3    C_PHP_R      0.013
## 4      EMC_L      0.014
## 5      EMC_R      0.012
## 6      FAT_L          0
## 7      FAT_R          0
## 8     IFOF_L      0.001
## 9     IFOF_R       0.02
## 10    MdLF_L       0.01
## 11     PAT_L       0.02
## 12     PAT_R      0.005
## 13    SLF2_L          0
## 14    SLF2_R          0
## 15    SLF3_L          0
## 16    SLF3_R          0
## 17     CBT_L      0.004
## 18     CBT_R          0
## 19   CPT_F_L          0
## 20   CPT_F_R          0
## 21   CPT_O_L      0.006
## 22   CPT_O_R      0.008
## 23    CS_A_L          0
## 24    CS_A_R          0
## 25    CS_P_R      0.007
## 26    CS_S_L          0
## 27    CS_S_R          0
## 28     CST_L      0.015
## 29     CST_R      0.022
## 30    DRTT_R          0
## 31     RST_L          0
## 32     RST_R          0
## 33    TR_A_L          0
## 34    TR_A_R          0
## 35    TR_P_L      0.027
## 36    TR_P_R      0.045
## 37    TR_S_L          0
## 38    TR_S_R          0
## 39        CC      0.001
```

```
#fdr corrected only dep network 10%
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$inDepNetwork_vector ==
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##              p_anova
## AF_L    1.091485e-05
## AF_R    2.467021e-03
## C_PHP_R 8.534313e-03
```

```
## FAT_L   3.504740e-09
## FAT_R   1.151864e-08
## MdLF_L  6.225199e-03
## MdLF_R  4.272190e-01
## SLF2_L  1.118391e-04
## SLF2_R  5.330751e-06
## SLF3_R  2.709435e-07
## CBT_L   1.905821e-03
## CBT_R   1.529588e-06
## CPT_O_R 5.241754e-03
## CS_P_R  4.292888e-03
## TR_P_R  3.710924e-02
```

```
print(fascicle_anova_fdr_association)
```

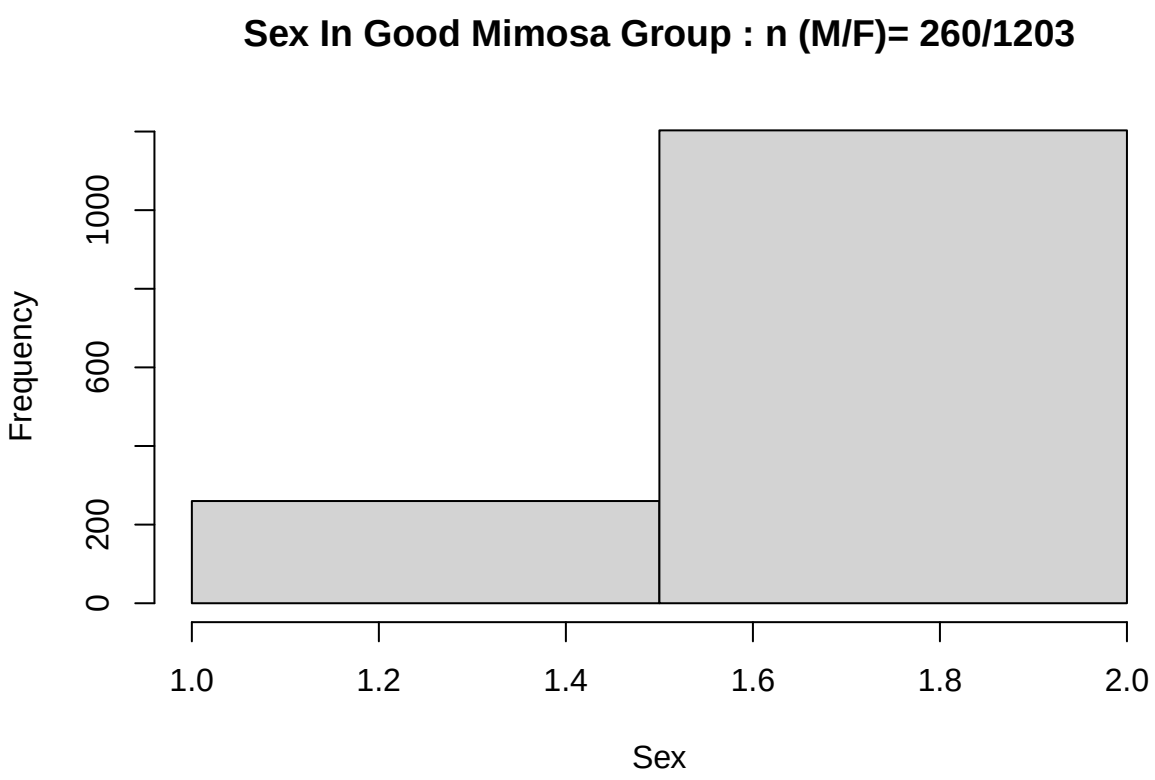
```
##    component p_FDR_corr
## 1       AF_L          0
## 2       AF_R      0.004
## 3    C_PHP_R       0.01
## 4      FAT_L          0
## 5      FAT_R          0
## 6     MdLF_L      0.008
## 7     SLF2_L          0
## 8     SLF2_R          0
## 9     SLF3_R          0
## 10     CBT_L      0.004
## 11     CBT_R          0
## 12   CPT_O_R      0.007
## 13    CS_P_R      0.006
## 14    TR_P_R       0.04
```

```
#uncorrected
fascicle_anova_mm_p <- sapply(fascicle_anova_mm, function(v) v$"Pr(>F)"[1])
fascicle_anova_mm_p05_unc <- as.data.frame(fascicle_anova_mm_p[fascicle_anova_mm_p < 0.05])
print(fascicle_anova_mm_p05_unc)
```

```
##         fascicle_anova_mm_p[fascicle_anova_mm_p < 0.05]
## AF_L                                        1.091485e-05
## AF_R                                        2.467021e-03
## C_FPH_L                                     4.984001e-02
## C_FP_L                                      3.886481e-03
## C_PHP_L                                     1.181989e-02
## C_PHP_R                                     8.534313e-03
## C_PH_R                                      3.252155e-02
## EMC_L                                       1.001833e-02
## EMC_R                                       8.104994e-03
## FAT_L                                       3.504740e-09
## FAT_R                                       1.151864e-08
## IFOF_L                                      2.634713e-04
## IFOF_R                                      1.480628e-02
## ILF_L                                       5.165942e-03
## MdLF_L                                      6.225199e-03
## PAT_L                                       1.514194e-02
```

```
## PAT_R                                  2.515301e-03
## SLF1_L                                 4.848380e-03
## SLF2_L                                 1.118391e-04
## SLF2_R                                 5.330751e-06
## SLF3_L                                 2.013766e-06
## SLF3_R                                 2.709435e-07
## UF_L                                   3.839107e-06
## UF_R                                   2.625400e-09
## VOF_R                                  7.899826e-03
## SCP                                    6.243069e-04
## AR_L                                   2.138359e-02
## CBT_L                                  1.905821e-03
## CBT_R                                  1.529588e-06
## CPT_F_L                                1.291364e-07
## CPT_F_R                                9.554555e-06
## CPT_O_L                                3.610910e-03
## CPT_O_R                                5.241754e-03
## CS_A_L                                 2.403762e-11
## CS_A_R                                 5.743437e-08
## CS_P_R                                 4.292888e-03
## CS_S_L                                 2.739498e-06
## CS_S_R                                 2.356204e-06
## CST_L                                  1.065456e-02
## CST_R                                  1.748282e-02
## DRTT_L                                 2.438658e-05
## DRTT_R                                 8.061692e-06
## OR_L                                   2.633757e-03
## OR_R                                   1.854511e-02
## RST_L                                  6.118111e-09
## RST_R                                  4.270105e-08
## TR_A_L                                 3.314413e-12
## TR_A_R                                 2.332114e-08
## TR_P_L                                 2.192477e-02
## TR_P_R                                 3.710924e-02
## TR_S_L                                 4.302964e-06
## TR_S_R                                 1.651505e-04
## AC                                     1.706126e-02
## CC                                     4.716604e-04
```

```r
############ sex effect whole group

#isolate out only the depressed group and healthy group
dep_and_healthy_groups_for_ICD_analysis <- df_demo_and_fascicles %>% filter(depGroupVar != 0)
#healthhy = 713, total n = 1106

#### sex histo ###
hist(dep_and_healthy_groups_for_ICD_analysis$sex_binarized,
main = paste0("Sex In Good Mimosa Group : n (M/F)= ", sum(dep_and_healthy_groups_for_ICD_analysis$sex_bi
```




```
#lm
fascicle_sex_lm <- lapply(fascicle_names, function(x)
{
  lmerTest::lmer(substitute(i ~ osex + (1|EMPI), list(i = as.name(x))), data = dep_and_healthy_groups_f
})
names(fascicle_sex_lm) <- fascicle_names

#anova
fascicle_sex_anova <- lapply(fascicle_sex_lm, anova)

#fdr corrected
fascicle_sex_anova_fdr <- fdr_anova_generic(fascicle_sex_anova, 1)
```

```
##             p_anova
## AF_L     0.69727078
## AF_R     0.82588275
## C_FPH_L  0.66663127
## C_FPH_R  0.78021064
## C_FP_L   0.77940408
## C_FP_R   0.96162552
## C_PH_L   0.77797392
## C_PHP_L  0.86187337
## C_PHP_R  0.10576254
## C_PH_R   0.14464902
## C_R_L    0.16469351
## C_R_R    0.72581649
```

```
## EMC_L    0.75635997
## EMC_R    0.96122478
## FAT_L    0.76993873
## FAT_R    0.74358206
## IFOF_L   0.63518098
## IFOF_R   0.28517254
## ILF_L    0.96931685
## ILF_R    0.33944754
## MdLF_L   0.61082462
## MdLF_R   0.98835150
## PAT_L    0.86851432
## PAT_R    0.61372991
## SLF1_L   0.43904219
## SLF1_R   0.58237690
## SLF2_L   0.47540258
## SLF2_R   0.83083937
## SLF3_L   0.50461083
## SLF3_R   0.54600740
## UF_L     0.86110344
## UF_R     0.78351520
## VOF_L    0.54093263
## VOF_R    0.92811368
## CB_L     0.48614318
## CB_R     0.70109488
## ICP_L    0.04752668
## ICP_R    0.02281144
## MCP      0.04178674
## SCP      0.03934122
## V        0.51312978
## CNIII_L  0.40863672
## CNIII_R  0.64009232
## CNII_L   0.24683773
## CNII_R   0.39759629
## CNVIII_L 0.10218918
## CNVIII_R 0.00294601
## CNVII_L  0.90413878
## CNVII_R  0.58623212
## CNV_L    0.62701707
## CNV_R    0.14551115
## AR_L     0.78087516
## AR_R     0.54728163
## CBT_L    0.88067883
## CBT_R    0.58631344
## CPT_F_L  0.80371334
## CPT_F_R  0.34175143
## CPT_O_L  0.53129724
## CPT_O_R  0.01705882
## CPT_P_L  0.37915277
## CPT_P_R  0.24846119
## CS_A_L   0.64025839
## CS_A_R   0.99071662
## CS_P_L   0.89724863
## CS_P_R   0.15085946
## CS_S_L   0.77830420
```

```
## CS_S_R   0.60956156
## CST_L    0.13912858
## CST_R    0.17348503
## DRTT_L   0.28466628
## DRTT_R   0.12683713
## F_L      0.10159578
## F_R      0.53312595
## ML_L     0.35814017
## ML_R     0.30312527
## OR_L     0.34785020
## OR_R     0.05669068
## RST_L    0.80759808
## RST_R    0.92364571
## TR_A_L   0.73648852
## TR_A_R   0.95220733
## TR_P_L   0.59857247
## TR_P_R   0.51062019
## TR_S_L   0.78928324
## TR_S_R   0.67489949
## AC       0.41529827
## CC       0.47081511
```

```
print(fascicle_sex_anova_fdr)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_sex_anova[which(fascicle_bundle_mapping$name_vector == "asso
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##           p_anova
## AF_L    0.6972708
## AF_R    0.8258827
## C_FPH_L 0.6666313
## C_FPH_R 0.7802106
## C_FP_L  0.7794041
## C_FP_R  0.9616255
## C_PH_L  0.7779739
## C_PHP_L 0.8618734
## C_PHP_R 0.1057625
## C_PH_R  0.1446490
## C_R_L   0.1646935
## C_R_R   0.7258165
## EMC_L   0.7563600
## EMC_R   0.9612248
## FAT_L   0.7699387
## FAT_R   0.7435821
## IFOF_L  0.6351810
## IFOF_R  0.2851725
## ILF_L   0.9693168
## ILF_R   0.3394475
## MdLF_L  0.6108246
```

```
## MdLF_R  0.9883515
## PAT_L   0.8685143
## PAT_R   0.6137299
## SLF1_L  0.4390422
## SLF1_R  0.5823769
## SLF2_L  0.4754026
## SLF2_R  0.8308394
## SLF3_L  0.5046108
## SLF3_R  0.5460074
## UF_L    0.8611034
## UF_R    0.7835152
## VOF_L   0.5409326
## VOF_R   0.9281137
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#visreg
#sapply(fascicle_sex_lm,visreg)
```

```
### This subscript compares proportion of fascicles lost for each fascicle of the 80+ between those in

#Of note, adding age into this model makes things WORSE

### Separately considers findings just within the association cortex
#isolate out only the depressed group and healthy group
df_mm <- df_demo_and_fascicles %>% filter(depGroupVar != 0)
#n depressed = 859, healthy = 604, total n = 1463


#lm
fascicle_lm_mm <- lapply(fascicle_names, function(x)
{
  lmerTest::lmer(substitute(i ~ depGroupVar + (1 | EMPI), list(i = as.name(x))), data = df_mm)
})
names(fascicle_lm_mm) <- fascicle_names

#anova
fascicle_anova_mm <- lapply(fascicle_lm_mm, anova)

#fdr corrected
fascicle_anova_mm_fdr <- fdr_anova_generic(fascicle_anova_mm, 1)
```

```
##             p_anova
## AF_L     0.13429335
## AF_R     0.03235420
## C_FPH_L  0.42628920
## C_FPH_R  0.33147011
## C_FP_L   0.28944293
## C_FP_R   0.88528985
```

```
## C_PH_L   0.34630808
## C_PHP_L  0.24680859
## C_PHP_R  0.46608068
## C_PH_R   0.93423558
## C_R_L    0.07767836
## C_R_R    0.85961964
## EMC_L    0.50067112
## EMC_R    0.38320193
## FAT_L    0.25566432
## FAT_R    0.03337075
## IFOF_L   0.28004535
## IFOF_R   0.13158605
## ILF_L    0.21509695
## ILF_R    0.09433817
## MdLF_L   0.26221335
## MdLF_R   0.47079167
## PAT_L    0.44943993
## PAT_R    0.11981933
## SLF1_L   0.22249684
## SLF1_R   0.19780905
## SLF2_L   0.43029064
## SLF2_R   0.04066933
## SLF3_L   0.82657447
## SLF3_R   0.09562107
## UF_L     0.42374962
## UF_R     0.28341051
## VOF_L    0.93124760
## VOF_R    0.11384038
## CB_L     0.84471206
## CB_R     0.67206062
## ICP_L    0.97520952
## ICP_R    0.57079652
## MCP      0.54875597
## SCP      0.97731157
## V        0.55621692
## CNIII_L  0.65588931
## CNIII_R  0.52101781
## CNII_L   0.32121681
## CNII_R   0.89486176
## CNVIII_L 0.68989818
## CNVIII_R 0.82108267
## CNVII_L  0.99488292
## CNVII_R  0.59205618
## CNV_L    0.33702345
## CNV_R    0.46751703
## AR_L     0.22948815
## AR_R     0.17141093
## CBT_L    0.17245719
## CBT_R    0.16960750
## CPT_F_L  0.16328658
## CPT_F_R  0.04932598
## CPT_O_L  0.04346334
## CPT_O_R  0.15704376
## CPT_P_L  0.26818520
```

```
## CPT_P_R  0.03471933
## CS_A_L   0.27996494
## CS_A_R   0.30276974
## CS_P_L   0.18979111
## CS_P_R   0.28887943
## CS_S_L   0.13056768
## CS_S_R   0.05780417
## CST_L    0.18007628
## CST_R    0.08842954
## DRTT_L   0.14843331
## DRTT_R   0.01914199
## F_L      0.31550873
## F_R      0.61942793
## ML_L     0.54420042
## ML_R     0.01259474
## OR_L     0.19090167
## OR_R     0.08906442
## RST_L    0.35489429
## RST_R    0.19845390
## TR_A_L   0.20299771
## TR_A_R   0.11080876
## TR_P_L   0.10429539
## TR_P_R   0.06339750
## TR_S_L   0.18879555
## TR_S_R   0.01724321
## AC       0.10599501
## CC       0.09939558
```

```
print(fascicle_anova_mm_fdr)#anova values < 0.05, uncorrected
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only association cortex
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$name_vector == "assoc
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.13429335
## AF_R    0.03235420
## C_FPH_L 0.42628920
## C_FPH_R 0.33147011
## C_FP_L  0.28944293
## C_FP_R  0.88528985
## C_PH_L  0.34630808
## C_PHP_L 0.24680859
## C_PHP_R 0.46608068
## C_PH_R  0.93423558
## C_R_L   0.07767836
## C_R_R   0.85961964
## EMC_L   0.50067112
## EMC_R   0.38320193
## FAT_L   0.25566432
```

```
## FAT_R   0.03337075
## IFOF_L  0.28004535
## IFOF_R  0.13158605
## ILF_L   0.21509695
## ILF_R   0.09433817
## MdLF_L  0.26221335
## MdLF_R  0.47079167
## PAT_L   0.44943993
## PAT_R   0.11981933
## SLF1_L  0.22249684
## SLF1_R  0.19780905
## SLF2_L  0.43029064
## SLF2_R  0.04066933
## SLF3_L  0.82657447
## SLF3_R  0.09562107
## UF_L    0.42374962
## UF_R    0.28341051
## VOF_L   0.93124760
## VOF_R   0.11384038
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only dep network
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$inDepNetwork_vector >0
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.13429335
## AF_R    0.03235420
## C_PHP_R 0.46608068
## EMC_L   0.50067112
## EMC_R   0.38320193
## FAT_L   0.25566432
## FAT_R   0.03337075
## IFOF_L  0.28004535
## IFOF_R  0.13158605
## ILF_R   0.09433817
## MdLF_L  0.26221335
## MdLF_R  0.47079167
## PAT_L   0.44943993
## PAT_R   0.11981933
## SLF2_L  0.43029064
## SLF2_R  0.04066933
## SLF3_L  0.82657447
## SLF3_R  0.09562107
## V       0.55621692
## AR_R    0.17141093
## CBT_L   0.17245719
## CBT_R   0.16960750
## CPT_F_L 0.16328658
```

```
## CPT_F_R 0.04932598
## CPT_O_L 0.04346334
## CPT_O_R 0.15704376
## CPT_P_L 0.26818520
## CPT_P_R 0.03471933
## CS_A_L  0.27996494
## CS_A_R  0.30276974
## CS_P_L  0.18979111
## CS_P_R  0.28887943
## CS_S_L  0.13056768
## CS_S_R  0.05780417
## CST_L   0.18007628
## CST_R   0.08842954
## DRTT_R  0.01914199
## ML_L    0.54420042
## RST_L   0.35489429
## RST_R   0.19845390
## TR_A_L  0.20299771
## TR_A_R  0.11080876
## TR_P_L  0.10429539
## TR_P_R  0.06339750
## TR_S_L  0.18879555
## TR_S_R  0.01724321
## CC      0.09939558
```

```
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```
#fdr corrected only dep network 10%
fascicle_anova_w_fiber_mapping <- fascicle_anova_mm[which(fascicle_bundle_mapping$inDepNetwork_vector ==
fascicle_anova_fdr_association <- fdr_anova_generic(fascicle_anova_w_fiber_mapping,1)
```

```
##            p_anova
## AF_L    0.13429335
## AF_R    0.03235420
## C_PHP_R 0.46608068
## FAT_L   0.25566432
## FAT_R   0.03337075
## MdLF_L  0.26221335
## MdLF_R  0.47079167
## SLF2_L  0.43029064
## SLF2_R  0.04066933
## SLF3_R  0.09562107
## CBT_L   0.17245719
## CBT_R   0.16960750
## CPT_O_R 0.15704376
## CS_P_R  0.28887943
## TR_P_R  0.06339750
```

```r
print(fascicle_anova_fdr_association)
```

```
## [1] component  p_FDR_corr
## <0 rows> (or 0-length row.names)
```

```r
#uncorrected
fascicle_anova_mm_p <- sapply(fascicle_anova_mm, function(v) v$"Pr(>F)"[1])
fascicle_anova_mm_p05_unc <- as.data.frame(fascicle_anova_mm_p[fascicle_anova_mm_p < 0.05])
print(fascicle_anova_mm_p05_unc)
```

```
##         fascicle_anova_mm_p[fascicle_anova_mm_p < 0.05]
## AF_R                                         0.03235420
## FAT_R                                        0.03337075
## SLF2_R                                       0.04066933
## CPT_F_R                                      0.04932598
## CPT_O_L                                      0.04346334
## CPT_P_R                                      0.03471933
## DRTT_R                                       0.01914199
## ML_R                                         0.01259474
## TR_S_R                                       0.01724321
```

Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the R code that generated the plot.