MAP: ABP and CBF/CVR
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Contents

```
######################################## File Directory #
platform <- sessionInfo()$platform

proj.dir <- file.path("~", "Documents", "BIOS7352", "Project1")
data.dir <- file.path(proj.dir, "dataForABP_CBF_2017-01-11.rds")

datfile <- file.path(data.dir)

###################################### Variables #

# Descriptive and Adjusting Variables
cov.con <- Cs(age, education)
cov.cat <- Cs(enrolled.dx.factor, sex.factor, raceethnicity.factor, apoe4pos.factor,
    enrolled.dx.factor, htnrx.factor, diabetes.factor, currentsmoking.factor,
    cvd.factor, afib.factor, echo.lvh.factor)

desc.cov <- c(cov.cat, cov.con)

# covariates for model
cov <- Cs(age, raceethnicity.factor, education, enrolled.dx.factor, apoe4pos.factor,
    icv)

# Predictors
predictors <- Cs(systolic.rising.surge, systolic.prewaking.surge, nocturnal.systolic.diff.sleep.self.report

# Outcomes
outcomes.reac <- Cs(asl.reac.left.hemisphere, asl.reac.right.hemisphere, asl.reac.left.frontal.lobe,
    asl.reac.right.frontal.lobe, asl.reac.frontal.lobe, asl.reac.left.occipital.lobe,
    asl.reac.right.occipital.lobe, asl.reac.occipital.lobe, asl.reac.left.temporal.lobe,
    asl.reac.right.temporal.lobe, asl.reac.temporal.lobe, asl.reac.left.parietal.lobe,
    asl.reac.right.parietal.lobe, asl.reac.parietal.lobe)
outcomes.reac = paste0(outcomes.reac, ".hct")

ma.vars <- Cs(ma.left.hemisphere, ma.right.hemisphere, ma.left.frontal.lobe.vol,
    ma.right.frontal.lobe.vol, ma.frontal.lobe.vol, ma.left.occipital.lobe.vol,
    ma.right.occipital.lobe.vol, ma.occipital.lobe.vol, ma.left.temporal.lobe.vol,
    ma.right.temporal.lobe.vol, ma.temporal.lobe.vol, ma.left.parietal.lobe.vol,
    ma.right.parietal.lobe.vol, ma.parietal.lobe.vol)

outcomes.list = vector("list", 1)
names(outcomes.list) = c("ASL.Reac")
outcomes.list[["ASL.Reac"]] = outcomes.reac

outcomes = unlist(outcomes.list)

# Exclusion Criteria Variables
excl.var <- Cs(time.reading.indicator, asl.reac.usable)
```

```
totalData <- readRDS(datfile)
```

1 Summary of Project Requests

1.1 Project Background

- Alzheimer's disease (AD) impairs short-term memory and affects one's ability to manage through daily life.
- Disease progresses from normal cognition through a stage of mild cognitive impairment (MCI) and finally to AD.
- Since there are currently no treatments for AD, research focuses on prevention and early detection so that effective strategies may be implemented once treatments are available.
- Cardiovascular measures may be associated with and useful in identifying early symptoms of AD.
- Cerebrovascular reactivity (CVR), possibly useful in early identification of patients at risk for AD, is a measurement of the change in cerebral blood flow when the vascular system is challenged by presence of carbon dioxide.
- The current project goal is to determine if there is an association between cardiovascular measures (based on ambulatory measurements of systolic blood pressure) and cerebrovascular reactivity.

1.2 Project Goals

Primary Aim

- Characterize the associations between ambulatory blood pressure measurements (ABPM) and cerebrovascular reactivity.
- **Hypothesis:** Patients with abnormal variability or surge patterns will be associated with decreased CVR.

Secondary Aim

- Investigate which ABPM predictor is most predictive of cognitive function, as measured by CVR.

2 Inclusion/Exclusion Criteria

```
##################################### Inclusion/Exclusion #

cvrdata <- totalData[totalData$asl.reac.usable == 1 & totalData$enrolled.dx.factor !=
    "Dementia", c(1:18, 61, grep("asl.reac", names(totalData)), grep("ma.",
    names(totalData)))]
names(cvrdata) <- sub("asl.reac.", "", names(cvrdata), fixed = TRUE)
names(cvrdata) <- sub(".hct", "", names(cvrdata), fixed = TRUE)
names(cvrdata) <- sub(".factor", "", names(cvrdata), fixed = TRUE)
names(cvrdata) <- sub("turnal.systolic.diff.sleep.self.reported", ".sys.diff",
    names(cvrdata), fixed = TRUE)
cvrdata <- cvrdata[cvrdata$time.reading.indicator == "Yes" & !is.na(cvrdata$time.reading.indicator),
    ]


exclude <- totalData[!(totalData$map.id %in% cvrdata$map.id), c(1:18, 61, grep("asl.reac",
    names(totalData)), grep("ma.", names(totalData)))]
names(exclude) <- sub("asl.reac.", "", names(exclude), fixed = TRUE)
names(exclude) <- sub(".hct", "", names(exclude), fixed = TRUE)
names(exclude) <- sub(".factor", "", names(exclude), fixed = TRUE)
names(exclude) <- sub("turnal.systolic.diff.sleep.self.reported", ".sys.diff",
    names(exclude), fixed = TRUE)
names(cvrdata$noc.sys.diff)
```

```
NULL
```

Comparison of included/excluded data

```
######################################## Inclusion/Exclusion Comparison #

cats <- names(cvrdata)[2:18]
comparison <- c(c(), c(), c(), c())
is <- length(cvrdata$map.id)
xs <- length(exclude$map.id)
for (cat in cats) {
    if (is.factor(cvrdata[, cat])) {
        chiData <- rbind(cbind(cvrdata[, cat], rep("is", length(cvrdata[, cat]))),
            cbind(exclude[, cat], rep("xs", length(exclude[, cat]))))
        pp <- chisq.test(table(chiData[, 1], chiData[, 2]))$p.value
        comparison <- rbind(comparison, c(label(cvrdata[, cat]), "", "", round(pp,
            4)))
        for (lev in levels(cvrdata[, cat])) {
            comparison <- rbind(comparison, c(paste("--", lev), paste(s <- sum(cvrdata[,
                cat] == lev, na.rm = T), " (", round(s * 100/is), "%)", sep = ""),
                paste(s <- sum(exclude[, cat] == lev, na.rm = T), " (", round(s *
                  100/xs), "%)", sep = ""), ""))
        }
        next
    }
    anovaData <- as.data.frame(rbind(cbind(cvrdata[, cat], rep("is", length(cvrdata[,
        cat]))), cbind(exclude[, cat], rep("xs", length(exclude[, cat])))))
    anovaData[, 1] <- as.numeric(as.character(anovaData[, 1]))
    pp <- kruskal.test(anovaData[, 1] ~ anovaData[, 2])$p.value
    comparison <- rbind(c(label(cvrdata[, cat]), paste(round(mean(cvrdata[,
        cat], na.rm = T), 1), " (", round(sd(cvrdata[, cat], na.rm = T), 1),
        ")", sep = ""), paste(round(mean(exclude[, cat], na.rm = T), 1), " (",
        round(sd(exclude[, cat], na.rm = T), 1), ")", sep = ""), round(pp, 4)),
```

```
        comparison)
}
comparison <- as.data.frame(comparison[, c(1, 3, 2, 4)])
colnames(comparison) <- c("Variable", "Excluded", "Analyzed Data", "P-Value")
kable(comparison, width = 3, caption = paste("Comparison of Demographics for Excluded & Included Data, w/ N
    length(exclude$map.id), " and N=", length(cvrdata$map.id), " respectively",
    sep = ""))
```

```
Error in kable_latex(x = structure(c("Diff.  in mean SBP, wake - sleep, self-reported periods", :
unused argument (width = 3)
```

3 Statistical Analysis Plan

3.1 Variables

Outcomes: CVR measures for different regions of interest within the brain

- `asl.reac.left.hemisphere.hct`
- `asl.reac.right.hemisphere.hct`
- `asl.reac.left.frontal.lobe.hct`
- `asl.reac.right.frontal.lobe.hct`
- `asl.reac.frontal.lobe.hct`
- `asl.reac.left.occipital.lobe.hct`
- `asl.reac.right.occipital.lobe.hct`
- `asl.reac.occipital.lobe.hct`
- `asl.reac.left.temporal.lobe.hct`
- `asl.reac.right.temporal.lobe.hct`
- `asl.reac.temporal.lobe.hct`
- `asl.reac.left.parietal.lobe.hct`
- `asl.reac.right.parietal.lobe.hct`
- `asl.reac.parietal.lobe.hct`

Predictors

- `systolic.prewaking.surge`: Mean SBP in two hours after self-reported wake time minus mean SBP in two hours prior to self-reported wake time
- `systolic.rising.surge`: First SBP reading after self-reported wake time minus last SBP before self-reported wake time
- `nocturnal.systolic.diff.sleep.self.reported`: Mean SBP during self-reported wake time minus mean SBP from self-reported asleep time

Covariates

- `age`*
- `education`*
- `sex.factor`*
- `enrolled.dx.factor`*: diagnosis group (dementia excluded)
  - Normal
  - MCI
  - Ambiguous at risk
- `raceethnicity.factor`*
- `apoe4pos.factor`*
- `htnrx.factor`*
- `diabetes.factor`

Diabetes?

Regional brain volume variables. Models for outcomes in a given region are controlled for the corresponding variable for volume in that region.

- ma.left.hemisphere.vol
- ma.right.hemisphere.vol
- ma.left.frontal.lobe.vol
- ma.right.frontal.lobe.vol
- ma.frontal.lobe.vol
- ma.left.occipital.lobe.vol
- ma.right.occipital.lobe.vol
- ma.occipital.lobe.vol
- ma.left.temporal.lobe.vol
- ma.right.temporal.lobe.vol
- ma.temporal.lobe.vol
- ma.left.parietal.lobe.vol
- ma.right.parietal.lobe.vol
- ma.parietal.lobe.vol

```
######################################## Missing Data #

missing <- c(c(), c())
# comparison[,c('Variable', 'Analyzed Data')]
for (cat in cats) {
    missing <- rbind(missing, c(label(cvrdata[, cat]), paste(s <- sum(is.na(cvrdata[,
        cat])), " (", round(s * 100/is, 2), "%)", sep = "")))
}

missing <- as.data.frame(missing)
colnames(missing) <- c("Variable", "Missingness")

print(xtable(missing, caption = paste("Missingness (N=", nrow(cvrdata), ")",
    sep = "")), caption.placement = "top")
```

3.2 Analysis Plan Overview

Cross-sectional analysis of 174 (check) patients from the VMAC MAP study.

certain covariates not included in models because essentially all patients were in one of the categories (e.g. smoking had like one non-smoker)

4 Descriptive Statistics

4.1 All variables

```
latex(describe(mydat0, descript = "All variables"), file = "")
```

```
Error in describe(mydat0, descript = "All variables"):  object 'mydat0' not found
```

Table 1: Missingness (N=174)

	Variable	Missingness
1	Consensus Decision for Diagnosis	0 (0%)
2	Sex	0 (0%)
3	Two-level race/ethnicity	0 (0%)
4	ApoE4+ (at least one E4 allele)	0 (0%)
5	Consensus Decision for Diagnosis	0 (0%)
6	Taking at least 1 anti-hypertensive med	0 (0%)
7	Diabetic, determined by a1c, glucose, and/or rx	0 (0%)
8	Current smoker (or quit in this or last calendar yr)	0 (0%)
9	CVD, determined from variables in med hx	0 (0%)
10	A-fib, determined by med hx and/or echo and/or cmr rhythm	0 (0%)
11	LV hypertrophy, determined by sex and scaled LV mass	1 (0.57%)
12	Age at medhx.date, recalculated	0 (0%)
13	Education (years)	0 (0%)
14	ICV (calculated)	0 (0%)
15	systolic.post.wake.1 minus systolic.pre.wake.1	23 (13.22%)
16	systolic.post.wake.mean minus systolic.pre.wake.mean	27 (15.52%)
17	Diff. in mean SBP, wake - sleep, self-reported periods	15 (8.62%)

```
my.LatexlTable <- function(my.descr.var, my.bygrp, my.bygrp.lab = NULL, my.dat,
    my.test = TRUE, my.overall = TRUE, printWarning = TRUE) {
    my.descr.var = setdiff(my.descr.var, my.bygrp)
    descrForm <- as.formula(paste0(paste(my.descr.var, collapse = " + "), "~",
        my.bygrp))

    summary = summaryM(descrForm, data = my.dat, test = my.test, continuous = 5,
        overall = my.overall)

    my.bygrp.lab = ifelse(is.na(my.bygrp.lab), my.bygrp, my.bygrp.lab)
    cat("\\LTcapwidth=\\textwidth \n")
    if (printWarning) {
        cat("\\textcolor{magenta}{Due to small cell counts, some of the chi-squared values and p-values may
    }

    latex(summary, file = "", what = "%", caption = paste0("All variables: Descriptive statistics by ",
        my.bygrp.lab), prn = TRUE, npct = "both", exclude1 = FALSE, prmsd = TRUE,
        long = TRUE, where = "htbp", digits = 3, pdig = 4, round = 2, size = "smaller[3]",
        outer.size = "footnotesize", lines.page = 400, middle.bold = TRUE, longtable = TRUE,
        center = "centering", label = paste0("tbl:descr.", my.bygrp), vnames = "names")
}
```

5 Analysis Results

Weighted vs closest for match?

I changed name of imputation to ‘impute.data‘ to avoid issue with there being a function called ‘impute‘

```
######################################## Multiple-Imputation #
label(cvrdata$enrolled.dx) <- "Diagnosis"
# toPredict <- c('systolic.rising.surge', 'systolic.prewaking.surge',
# 'noc.sys.diff')
```

```r
cvrdata$enrolled.dx <- factor(cvrdata$enrolled.dx)


impute.data <- aregImpute(~systolic.rising.surge + systolic.prewaking.surge +
    noc.sys.diff + enrolled.dx + sex + raceethnicity + apoe4pos + enrolled.dx +
    education + htnrx + icv + left.hemisphere + right.hemisphere, data = cvrdata,
    match = "closest")
```

imputation graphs will go in sensitivity analysis section

```r
######################################## Model Fitting #
outcomes.reac <- sub("asl.reac.", "", outcomes.reac, fixed = TRUE)
outcomes.reac <- sub(".hct", "", outcomes.reac, fixed = TRUE)



modelFit <- function(outcome, predictor, ma, knot) {

    fit <- fit.mult.impute(as.formula(paste0(outcome, "~ rcs(", predictor, ", c(",
        knot[1], ",", knot[2], ",", knot[3], ",", knot[4], ")) +", ma, "+",
        "age + sex + raceethnicity + education + enrolled.dx + apoe4pos")),
        fitter = ols, xtrans = impute.data, data = cvrdata)

    return(fit)
}

# Knot locations for each predictor
prewaking.knot <- c(0, quantile(subset(cvrdata, systolic.prewaking.surge > 0)$systolic.prewaking.surge,
    probs = c(0.25, 0.5, 0.75), na.rm = T))

rising.knot <- c(0, quantile(subset(cvrdata, systolic.rising.surge > 0)$systolic.rising.surge,
    probs = c(0.25, 0.5, 0.75), na.rm = T))

noc.knot <- c(0, quantile(subset(cvrdata, noc.sys.diff > 0)$noc.sys.diff, probs = c(0.1,
    0.5, 0.9), na.rm = T))

knots <- rbind(prewaking.knot, rising.knot, noc.knot)
colnames(knots) = NULL
knots

# Systolic prewaking surge
mod.sys.prewaking.surge <- list()
for (i in seq_along(outcomes.reac)) {
    mod.sys.prewaking.surge[[i]] <- modelFit(outcome = outcomes.reac[i], predictor = "systolic.prewaking.su
        ma = ma.vars[i], knot = prewaking.knot)
}

# Systolic rising surge
mod.sys.rising.surge <- list()
for (i in seq_along(outcomes.reac)) {
    mod.sys.rising.surge[[i]] <- modelFit(outcome = outcomes.reac[i], predictor = "systolic.rising.surge",
        ma = ma.vars[i], knot = rising.knot)
}

# Nocturnal Difference
mod.noc.sys.diff <- list()
for (i in seq_along(outcomes.reac)) {
```

```
    mod.noc.sys.diff[[i]] <- modelFit(outcome = outcomes.reac[i], predictor = "noc.sys.diff",
        ma = ma.vars[i], knot = noc.knot)
}
```

5.1 Test of Association between ABPM and CVR

Fit linear models with rcs for predictor to allow for non-linear association. Knots placed at 0 and other percentiles. 4 knots for each

```
outcomeNames <- c("Left Hemisphere", "Right Hemisphere", "Left Frontal Lobe",
    "Right Frontal Lobe", "Full Frontal Lobe", "Left Occipital Lobe", "Right Occipital Lobe",
    "Full Occipital Lobe", "Left Temporal Lobe", "Right Temporal Lobe", "Full Temporal Lobe",
    "Left Parietal Lobe", "Right Parietal Lobe", "Full Parietal Lobe")



sys.prewaking.pval <- lapply(mod.sys.prewaking.surge, function(x) anova(x)["systolic.prewaking.surge",
    "P"])
sys.rising.pval <- lapply(mod.sys.rising.surge, function(x) anova(x)["systolic.rising.surge",
    "P"])
noc.sys.diff.pval <- lapply(mod.noc.sys.diff, function(x) anova(x)["noc.sys.diff",
    "P"])

assoc.table <- data.frame(`SBP Prewaking Surge` = unlist(sys.prewaking.pval),
    `SBP Rising Surge` = unlist(sys.rising.pval), `Nocturnal SBP Difference` = unlist(noc.sys.diff.pval),
    row.names = outcomeNames, check.names = FALSE)

print(xtable(assoc.table, digits = 3, caption = "P-values for test of association between ABPM and CVR"),
    caption.placement = "top")
```

Table 2: P-values for test of association between ABPM and CVR

	SBP Prewaking Surge	SBP Rising Surge	Nocturnal SBP Difference
Left Hemisphere	0.166	0.665	0.096
Right Hemisphere	0.386	0.593	0.161
Left Frontal Lobe	0.295	0.537	0.088
Right Frontal Lobe	0.434	0.487	0.171
Full Frontal Lobe	0.369	0.496	0.105
Left Occipital Lobe	0.086	0.526	0.222
Right Occipital Lobe	0.524	0.300	0.044
Full Occipital Lobe	0.201	0.365	0.098
Left Temporal Lobe	0.840	0.962	0.313
Right Temporal Lobe	0.750	0.950	0.820
Full Temporal Lobe	0.827	0.968	0.617
Left Parietal Lobe	0.113	0.325	0.193
Right Parietal Lobe	0.283	0.484	0.150
Full Parietal Lobe	0.163	0.351	0.151

- The only model with an association detected at the 0.05 significance level was for nocturnal difference in systolic blood pressure.
- However, we would recommend a multiple comparisons adjustement for fitting the 42 models (e.g. using a Bonferroni-corrected significance level of $\frac{.05}{42} = .0012$). With an adjusted significance level, we would not see a significant association for any brain region-predictor of interest pair.

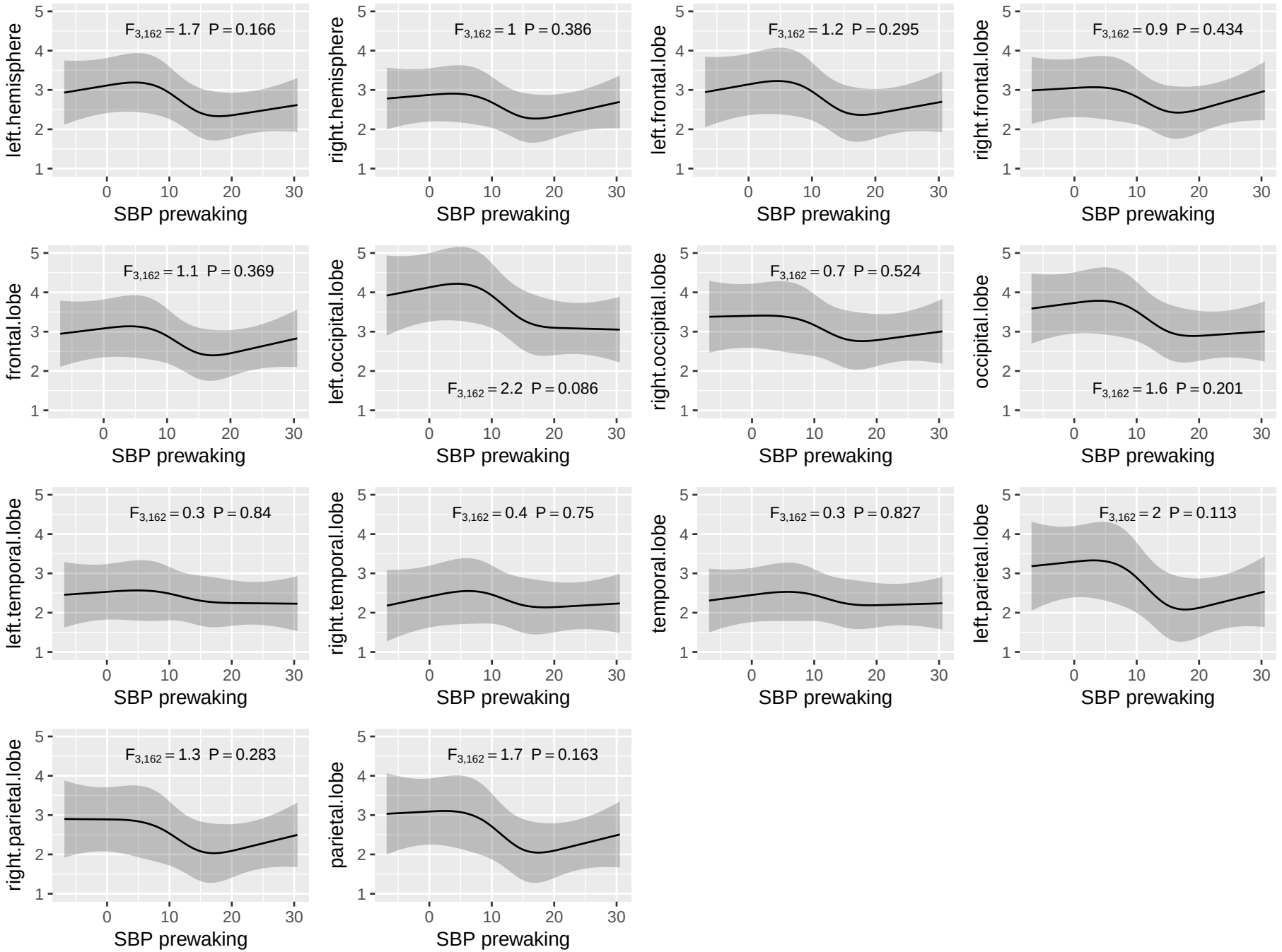
5.2 Coefficients and Partial Effect Plots

```
sys.prewaking.coef <- do.call(rbind, lapply(mod.sys.prewaking.surge, function(x) x$coef[grep("systolic",
    names(x$coef))]))

sys.rising.coef <- do.call(rbind, lapply(mod.sys.prewaking.surge, function(x) x$coef[grep("systolic",
    names(x$coef))]))

noc.diff.coef <- do.call(rbind, lapply(mod.sys.prewaking.surge, function(x) x$coef[grep("noc",
    names(x$coef))]))


coef.table <- data.frame(`SBP Prewaking Surge` = unlist(sys.prewaking.pval),
    `SBP Rising Surge` = unlist(sys.rising.pval), `Nocturnal SBP Difference` = unlist(noc.sys.diff.pval),
    row.names = outcomeNames, check.names = FALSE)

print(xtable(assoc.table, digits = 3, caption = "P-values for test of association between ABPM and CVR"),
    caption.placement = "top")
```

Since coefficients from fitting a cubic spline are not directly interpretable, we provide partial effect plots. A single plot is presented from each model for the predictor of interest against the CVR outcome for the specified region of interest. Parital effect plots show the effect of each SBP measure on CVR outcome with other variables in the model fixed. By default, continuous variables are fixed at their median and categorical variables are fixed at their reference group. For these data, the default plotting values for (non-brain volume) covariates are:

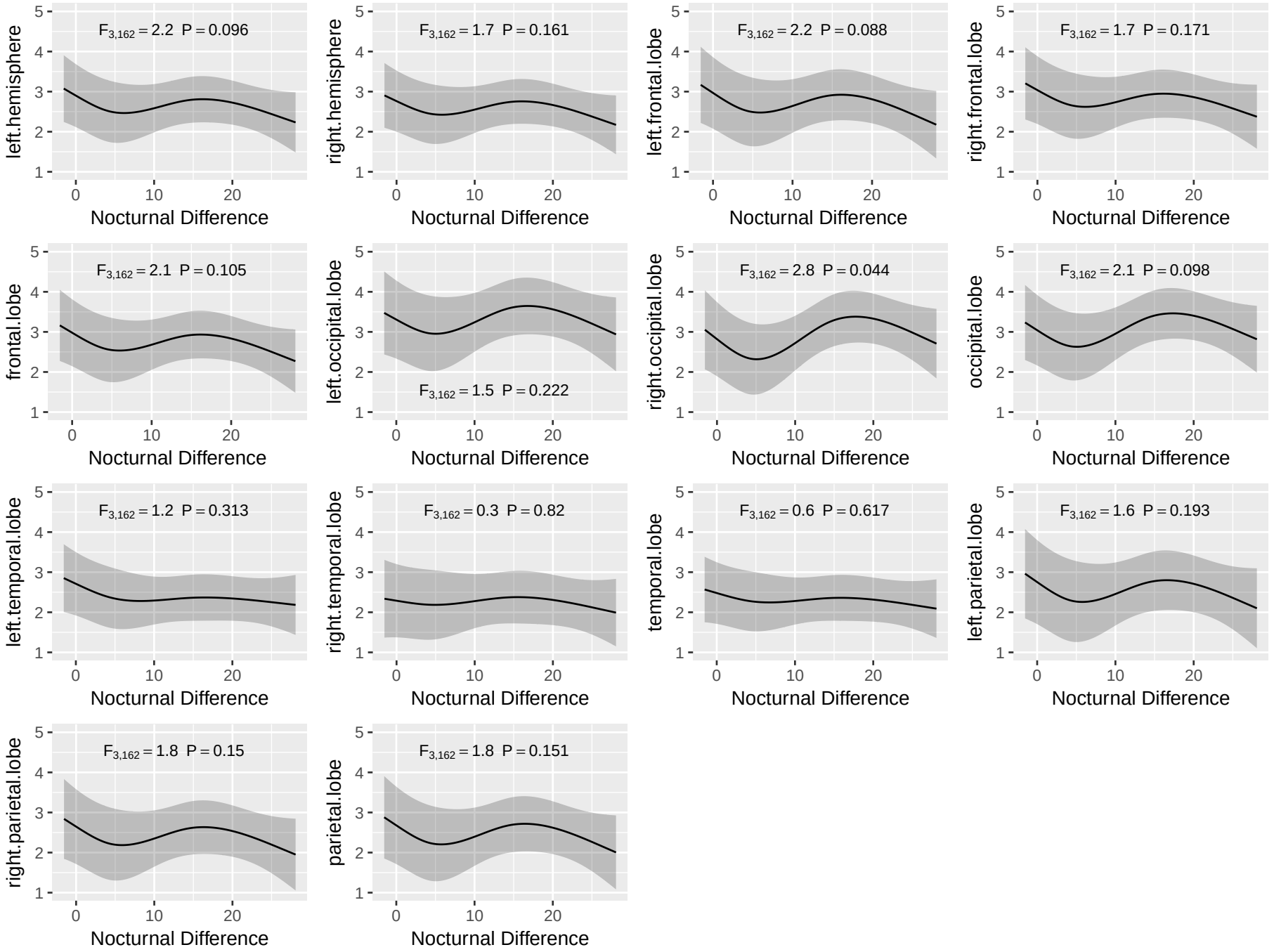
```
subset_cvrdata <- subset(cvrdata, select = c(age, sex, enrolled.dx, raceethnicity,
    apoe4pos, htnrx, education))
datadist(subset_cvrdata)$limits["Adjust to", ]
```

```
          age  sex enrolled.dx      raceethnicity apoe4pos htnrx education
Adjust to  73 Male      Normal Non-Hispanic White       No   Yes        16
```


left.hemisphere
$F_{3,162} = 1.7$ $P = 0.166$
right.hemisphere
$F_{3,162} = 1$ $P = 0.386$
left.frontal.lobe
$F_{3,162} = 1.2$ $P = 0.295$
right.frontal.lobe
$F_{3,162} = 0.9$ $P = 0.434$
frontal.lobe
$F_{3,162} = 1.1$ $P = 0.369$
left.occipital.lobe
$F_{3,162} = 2.2$ $P = 0.086$
right.occipital.lobe
$F_{3,162} = 0.7$ $P = 0.524$
occipital.lobe
$F_{3,162} = 1.6$ $P = 0.201$
left.temporal.lobe
$F_{3,162} = 0.3$ $P = 0.84$
right.temporal.lobe
$F_{3,162} = 0.4$ $P = 0.75$
temporal.lobe
$F_{3,162} = 0.3$ $P = 0.827$
left.parietal.lobe
$F_{3,162} = 2$ $P = 0.113$
right.parietal.lobe
$F_{3,162} = 1.3$ $P = 0.283$
parietal.lobe
$F_{3,162} = 1.7$ $P = 0.163$
SBP prewaking

```r
# Systolic rising surge
sys.rising.PEP <- lapply(mod.sys.rising.surge, function(x) ggplot(Predict(x,
    systolic.rising.surge), adj.subtitle = FALSE, anova = anova(x), size.anova = 3,
    pval = TRUE, ylim. = c(1, 5), xlab = "SBP rising"))
do.call(grid.arrange, sys.rising.PEP)
```

```r
# Nocturnal difference
noc.sys.diff.PEP <- lapply(mod.noc.sys.diff, function(x) ggplot(Predict(x, noc.sys.diff),
    adj.subtitle = FALSE, anova = anova(x), size.anova = 3, pval = TRUE, ylim. = c(1,
        5), xlab = "Nocturnal Difference"))
do.call(grid.arrange, noc.sys.diff.PEP)
```

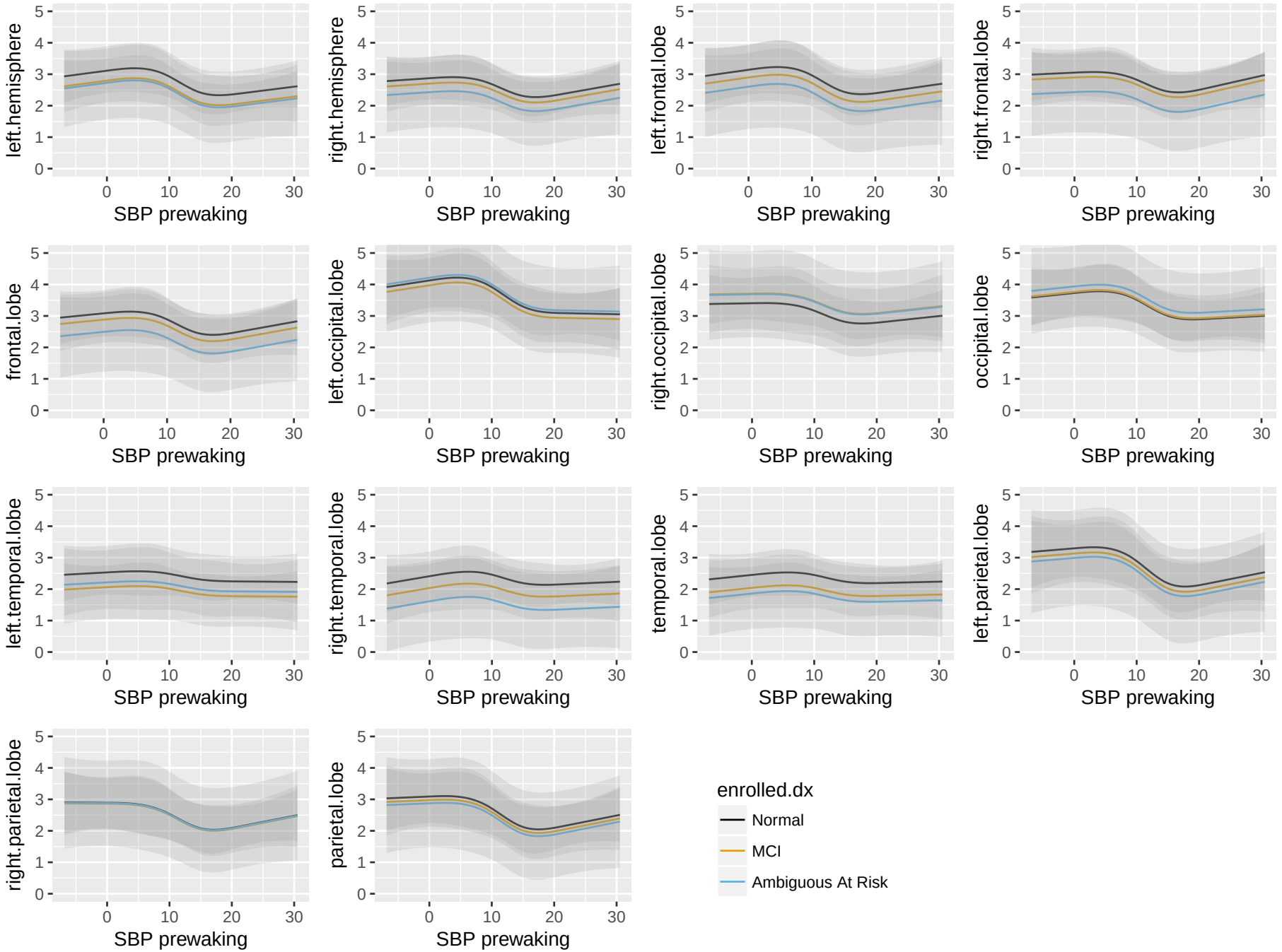

left.hemisphere
$F_{3,162} = 2.2$ P = 0.096
right.hemisphere
$F_{3,162} = 1.7$ P = 0.161
left.frontal.lobe
$F_{3,162} = 2.2$ P = 0.088
right.frontal.lobe
$F_{3,162} = 1.7$ P = 0.171
frontal.lobe
$F_{3,162} = 2.1$ P = 0.105
left.occipital.lobe
$F_{3,162} = 1.5$ P = 0.222
right.occipital.lobe
$F_{3,162} = 2.8$ P = 0.044
occipital.lobe
$F_{3,162} = 2.1$ P = 0.098
left.temporal.lobe
$F_{3,162} = 1.2$ P = 0.313
right.temporal.lobe
$F_{3,162} = 0.3$ P = 0.82
temporal.lobe
$F_{3,162} = 0.6$ P = 0.617
left.parietal.lobe
$F_{3,162} = 1.6$ P = 0.193
right.parietal.lobe
$F_{3,162} = 1.8$ P = 0.15
parietal.lobe
$F_{3,162} = 1.8$ P = 0.151
Nocturnal Difference
0
10
20
1
2
3
4
5

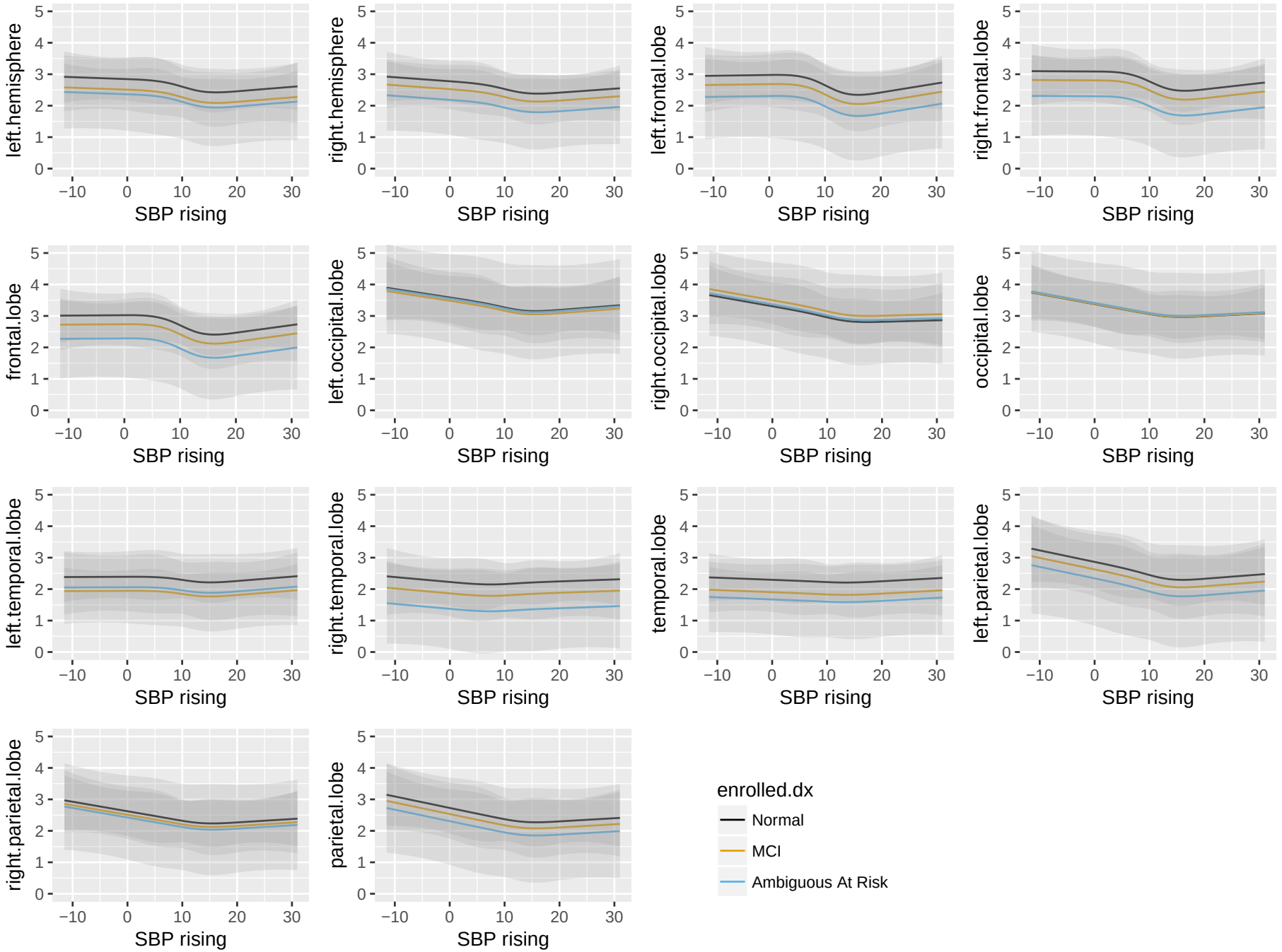
```
# All the above are at default values, but can look at these interactively
plot1 <- ggplot(Predict(mod.sys.prewaking.surge[[1]], systolic.prewaking.surge,
    age = c(60, 70)))
# plot2 <-
ggplot(Predict(mod.sys.prewaking.surge[[1]], systolic.prewaking.surge, enrolled.dx = c("Normal",
    "MCI", "Ambiguous At Risk"), age = dd$limits["Adjust to", "age"]))
grid.arrange(plot1, plot2, ncol = 2)

ggplot(Predict(mod.sys.prewaking.surge[[1]], systolic.prewaking.surge))

ggplot(Predict(mod.noc.sys.diff[[1]], noc.sys.diff)) + scale_x_discrete(limits = c(noc.knot,
    10, 20))
```

5.3 Partial Effect Plots: Stratified by Diagnosis

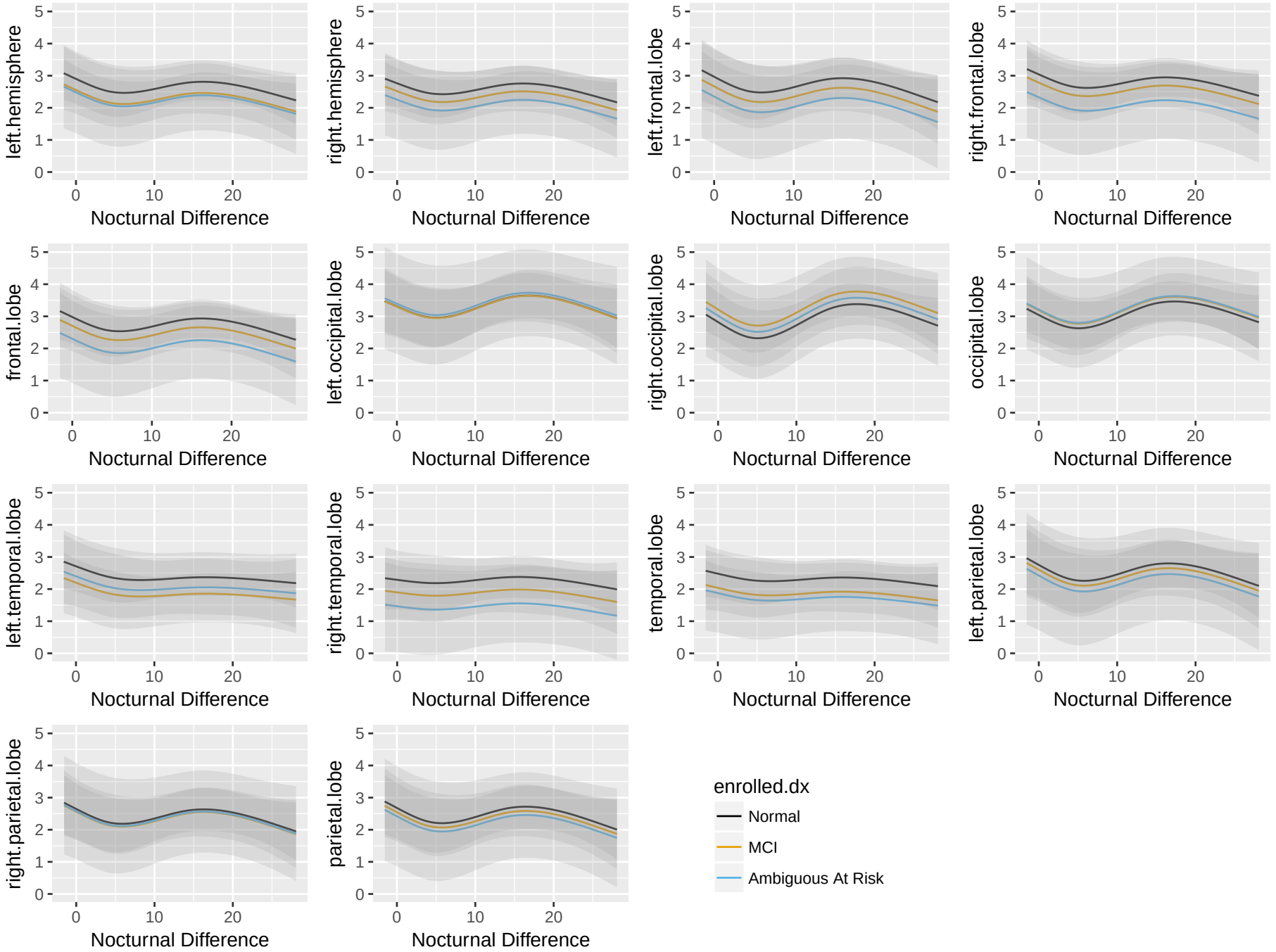
Though results weren't significant, to understand potential trends we also present partial effect plots stratified by diagnosis group

```
dd <- datadist(cvrdata)
options(datadist = "dd")
# Function obtained from:
# http://stackoverflow.com/questions/11883844/inserting-a-table-under-the-legend-in-a-ggplot2-histogram

# create inset table
g_legend <- function(a.gplot) {
    tmp <- ggplot_gtable(ggplot_build(a.gplot))
    leg <- which(sapply(tmp$grobs, function(x) x$name) == "guide-box")
    legend <- tmp$grobs[[leg]]
    return(legend)
}

legend.dx <- g_legend(ggplot(Predict(mod.noc.sys.diff[[1]], noc.sys.diff, enrolled.dx = c("Normal",
    "MCI", "Ambiguous At Risk"))))
```


left.hemisphere
right.hemisphere
left.frontal.lobe
right.frontal.lobe
frontal.lobe
left.occipital.lobe
right.occipital.lobe
occipital.lobe
left.temporal.lobe
right.temporal.lobe
temporal.lobe
left.parietal.lobe
right.parietal.lobe
parietal.lobe
SBP prewaking
0
10
20
30
1
2
3
4
5
enrolled.dx
Normal
MCI
Ambiguous At Risk


left.hemisphere
right.hemisphere
left.frontal.lobe
right.frontal.lobe
frontal.lobe
left.occipital.lobe
right.occipital.lobe
occipital.lobe
left.temporal.lobe
right.temporal.lobe
temporal.lobe
left.parietal.lobe
right.parietal.lobe
parietal.lobe
SBP rising
enrolled.dx
Normal
MCI
Ambiguous At Risk

```r
# Nocturnal difference
noc.sys.diff.PEP.dx <- lapply(mod.noc.sys.diff, function(x) ggplot(Predict(x,
    noc.sys.diff, enrolled.dx = c("Normal", "MCI", "Ambiguous At Risk")), colfill = "grey60",
    adj.subtitle = FALSE, ylim. = c(0, 5), xlab = "Nocturnal Difference") +
    theme(legend.position = "none"))


noc.sys.diff.PEP.dx[[15]] <- legend.dx
do.call(grid.arrange, noc.sys.diff.PEP.dx)
```


left.hemisphere
right.hemisphere
left.frontal.lobe
right.frontal.lobe
frontal.lobe
left.occipital.lobe
right.occipital.lobe
occipital.lobe
left.temporal.lobe
right.temporal.lobe
temporal.lobe
left.parietal.lobe
right.parietal.lobe
parietal.lobe
Nocturnal Difference
0
10
20
0
1
2
3
4
5
enrolled.dx
Normal
MCI
Ambiguous At Risk

5.4 Tests of Linearity for ABPM Measures

```
sys.prewaking.nonlin <- lapply(mod.sys.prewaking.surge, function(x) anova(x)[" Nonlinear",
    "P"])
sys.rising.nonlin <- lapply(mod.sys.rising.surge, function(x) anova(x)[" Nonlinear",
    "P"])
noc.sys.diff.nonlin <- lapply(mod.noc.sys.diff, function(x) anova(x)[" Nonlinear",
    "P"])


linear.table <- data.frame(`SBP Prewaking Surge` = unlist(sys.prewaking.nonlin),
    `SBP Rising Surge` = unlist(sys.rising.nonlin), `Nocturnal SBP Difference` = unlist(noc.sys.diff.nonlin
    row.names = outcomeNames, check.names = FALSE)

print(xtable(linear.table, digits = 3, caption = "P-values for test of linearity for ABPM predictors"),
    caption.placement = "top")
```

Table 3: P-values for test of linearity for ABPM predictors

	SBP Prewaking Surge	SBP Rising Surge	Nocturnal SBP Difference
Left Hemisphere	0.171	0.687	0.153
Right Hemisphere	0.267	0.669	0.215
Left Frontal Lobe	0.237	0.456	0.132
Right Frontal Lobe	0.281	0.519	0.231
Full Frontal Lobe	0.259	0.465	0.150
Left Occipital Lobe	0.274	0.632	0.136
Right Occipital Lobe	0.540	0.671	0.018
Full Occipital Lobe	0.333	0.591	0.047
Left Temporal Lobe	0.839	0.867	0.387
Right Temporal Lobe	0.551	0.854	0.736
Full Temporal Lobe	0.697	0.887	0.658
Left Parietal Lobe	0.179	0.546	0.182
Right Parietal Lobe	0.291	0.613	0.171
Full Parietal Lobe	0.211	0.556	0.155

6 Summary of Results

- Any associations?
- Trends observed in the partial effect plots?
- Nonlinearity of ABPM predictors?
- Secondary aim: predictive power of ABPM measures?

7 R session information

```
# helpful code from Nate (modified)
cat(version["version.string"][[1]], "\n")
```

```
R version 3.3.2 (2016-10-31)
```

```
pack <- installed.packages()
pack.out <- pack[, c("Package", "Version", "Priority", "Depends")]
pack.in.session <- (.packages())
pack.out2 <- data.frame(pack.out[pack.out[, 1] %in% pack.in.session, ])[, -1]
cat("Packages:\n")
```

```
Packages:
```

```
pack.out2[!pack.out2$Priority %in% c("base", "recommended"), -2, drop = FALSE]
```

```
          Version
Formula     1.2-1
ggplot2     2.2.1
gridExtra   2.2.1
Hmisc       4.0-2
knitr      1.15.1
rms         5.1-0
SparseM      1.72
xtable      1.8-2
                                                                        Depends
Formula                                                        R (>= 2.0.0), stats
ggplot2                                                                R (>= 3.1)
gridExtra                                                                  <NA>
Hmisc                        lattice, survival (>= 2.40-1), Formula, ggplot2 (>= 2.2)
knitr                                                                  R (>= 3.1.0)
rms       Hmisc (>= 4.0-2), survival (>= 2.40-1), lattice, ggplot2 (>=\n2.2), SparseM
SparseM                                                        R (>= 2.15), methods
xtable                                                                 R (>= 2.10.0)
```

8 Roles and Responsibilities

9 Code Appendix

Change this to echo = TRUE to print all code here in the appendix rather than in the report itself