Plots

Contents

Intro

This document illustrates the process used to create Figures 2-4 in from the paper *Genetic and morphological estimates of androgen exposure predict social deficits in multiple neurodevelopmental disorder cohorts.* These figures and data relate only to the study's DevGenes cohort, as raw data from the other cohort — SPARK – cannot be publicly released. SPARK data may be obtained by researchers approved by the Simons Foundation Autism Research Initiative, through SFARI Base: https://www.sfari.org/resource/sfari-base.

All code referenced in this document can be found in either `helper_functions.R` or `devGenes_final_figures_code.R`, and the data on which they are based can be found in `table_S1_final.txt` and `devGenes_final_factor_model_loadings.txt`.

Helper Functions

`img()`: A wrapper to make image() more convenient

```
img = function(x,ylab,xlab,axes,col,na.zero=F,breaks,do.breaks=T,...){
 cc = colorRampPalette(c("black","chartreuse"))
 if(any(x<0) & any(x>0)){
    cc = colorRampPalette(c("royalblue","royalblue4","black","orangered","goldenrod1"))
 }
 if(missing(ylab)) ylab=""
 if(missing(xlab)) xlab=""
 if(missing(axes)) axes=F
 if(missing(col)) col=cc(256)
 if(na.zero) x[is.na(x)] = 0
 if(do.breaks & missing(breaks)){
  mx = max(abs(x))
  qt = max(abs(quantile(x,c(0.01,0.99))))
  bk = c(-1*mx,seq(-1*qt,qt,length.out=255),mx)
  image(0:ncol(x),0:nrow(x),t(x),ylim=c(nrow(x),0),ylab=ylab,
   xlab=xlab,axes=axes,col=col,breaks=bk,...)
 }else{
 image(0:ncol(x),0:nrow(x),t(x),ylim=c(nrow(x),0),ylab=ylab,
  xlab=xlab,axes=axes,col=col,breaks=breaks,...)
 }
 box()
}
```

`bootlM()` and `lboot()`: wrappers for bootstrapping to get confidence intervals

```r
bootlM = function(x,y){
 keep = !is.na(x) & !is.na(y)
 x0 = x[keep]
 y0 = y[keep]
 these = sample(length(x0),replace=T)
 x0 = x0[these]
 y0 = y0[these]

 approx(lowess(x0,y0),xout=seq(0,80,1),rule=2)$y
}

### with input x and y, generate a lowess trend with 95% confidence intervals
lboot = function(x,y,subset,nboot=1000,return.boot=F){
 if(length(x)!=length(y)) stop("x and y have different lengths")
 if(missing(subset)){
  subset=1:length(x)
 }
 x = x[subset]
 y = y[subset]

 ### generate nboot lowess fits
 b = replicate(nboot,bootlM(x,y))

 qu = apply(b,1,quantile,0.975)
 ql = apply(b,1,quantile,0.025)
 qm = rowMeans(b)
 xq = 0:80

 out = list()
 out$x = xq
 out$y = qm
 out$ci = list(upr=qu,lwr=ql)
 out$points = list(x=x,y=y)
 if(return.boot){
  out$boot = b
 }
 return(out)
}
```

plotl(): A function to plot the output of lboot()

```
plotl = function(obj,pt.col,l.col,shade.col,plot.points=F,xlim=c(0,80),
    ylim,add=F,plot.ci=T,...){
 if(missing(ylim)){
  ylim=range(obj$y,na.rm=T)
  ylim = (c(-1,1)*abs(diff(ylim))) + ylim
 }
 if(!add){
  plot(obj,xlim=xlim,ylim=ylim,xlab="age (years)",type='l',col=l.col,...)
  if(plot.ci){
   polygon(c(obj$x,rev(obj$x)),c(obj$ci$lwr,rev(obj$ci$upr)),col=shade.col,border=l.col)
  }
 }else{
  lines(obj,col=l.col,...)
  if(plot.ci){
   polygon(c(obj$x,rev(obj$x)),c(obj$ci$lwr,rev(obj$ci$upr)),col=shade.col,border=l.col)
  }
 }
 if(plot.points){
  points(obj$points,pch=16,col=pt.col)
 }

}
```

The Data

Table 1: Factor Loadings

	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6	Factor7	Factor8	Factor9	Factor10	Factor11
social.eyecontact	0.1086367	0.4292602	0.0736042	0.1643372	0.1736255	0.2835086	0.3685458	0.0500302	0.3016591	-0.0381764	-0.1280986
social.init_conv	0.2852887	0.1512008	-0.0289435	0.2374517	0.1630843	0.1924666	0.3787394	0.1478946	0.3381085	-0.1800359	-0.0218842
social.uncomf_interact	0.0323974	0.1196371	0.1070747	0.0389679	0.1181215	-0.0130980	0.7039691	0.0786045	0.1543321	0.1342962	0.1714935
social.socializes	0.3813110	0.1493706	0.0620354	0.1495534	0.1271815	0.2526992	0.2149606	0.1206623	0.6884145	0.1012796	0.0045308
social.friends	0.3434447	0.1418500	0.0275180	0.2335482	0.1205117	0.2219378	0.3614091	0.0736616	0.4371931	0.0024861	0.1186012
social.soc_distress	0.1096375	0.4893621	0.1654568	0.2474608	0.1396017	0.0147531	0.2339567	0.3326524	0.1006547	0.2147951	0.0654177
rrb.rep_movies_music	0.1670886	0.2920419	-0.0919332	0.2194842	0.0383111	0.3441104	0.0827352	0.0789571	0.0574445	0.0407191	0.2013055
rrb.stim	0.0940111	0.0946858	0.1010345	0.1692635	0.0848560	0.6685771	-0.0039240	0.0493594	0.0793625	0.0849339	0.0940771
rrb.odd_beh	0.1920686	0.1746066	0.0410817	0.1308004	0.1261518	0.6093322	0.1252416	0.1198064	0.1153548	0.0220056	-0.0016797
rrb.needs_order	0.1072012	0.5804600	0.1458211	0.1302481	0.1316813	0.4224700	0.1504641	0.0069998	0.0805807	-0.0668679	0.0391601
rrb.mann_dis	0.2085801	0.4004670	0.2380111	0.2814674	0.1339018	0.2065598	0.1224160	0.2120164	0.2078487	-0.0718538	0.0339855
acad_abil.reading	0.7848285	-0.0728949	0.0362335	-0.0035160	0.0639259	0.0002604	0.0412783	0.1181537	-0.0802478	-0.0071809	0.0419540
acad_abil.writing	0.7846123	-0.0081306	0.0607637	0.1270829	0.0435566	0.1352355	0.0993364	0.0671456	0.0394453	0.0315433	0.0119071
acad_abil.math	0.7563774	-0.0338151	0.0059640	0.0075421	-0.0136599	0.0259029	-0.0296449	0.0331907	0.0727043	0.0293438	0.0651270
acad_abil.learn_new	0.7870456	0.0843797	0.0244262	0.1027442	0.0682323	0.2443105	0.0618290	0.0465394	0.1059697	0.0560536	0.0777145
language_level	0.3400045	0.0130433	0.0216755	0.0084760	0.0450168	-0.0001328	0.0560722	-0.0791267	0.1504180	0.0417985	-0.0546323
sensory.hugs	0.1222776	0.2781454	0.0307162	0.0001138	0.0805599	0.1131940	0.4283590	-0.0150713	0.0113038	0.0459380	-0.0261927
sensory.dizzy	0.0384089	0.2590796	0.0094119	-0.0782908	0.0850323	-0.0267729	-0.0426067	0.0648256	0.0563114	0.4826593	-0.0125189
sensory.clothing_atypical_temp	-0.0390338	0.3678003	0.1262807	0.1767642	0.1084653	0.2196858	0.1698069	0.0433369	0.0212022	0.1592841	0.0179347
sensory.haircut	0.2101859	0.1548386	0.0864475	0.4056075	0.0711193	0.1067211	-0.0284708	0.2599561	0.0451728	-0.1783465	0.1346923
sensory.sound	0.1398517	0.4147963	0.0862448	0.1823873	0.1136146	0.1883913	0.1382956	0.0570491	-0.0051759	-0.0393394	0.7303652
sensory.light	-0.0252027	0.4886829	0.1337168	0.1389714	0.1124484	0.0124121	0.1744358	0.0888327	0.0354690	0.1784304	0.2433216
sensory.odors	-0.0355109	0.6244332	0.2799430	-0.0409266	-0.0500753	-0.0192315	0.0718177	-0.0431105	0.0257336	0.2679002	0.1102792
sensory.tags	-0.1265136	0.5004148	0.0504564	0.1201747	0.0787497	0.0966972	0.0325400	0.0221242	0.0279833	0.0652394	0.0333144
sensory.sensory_distress	0.0684386	0.4845109	0.2534815	0.3501328	0.1500137	0.3044825	0.1266181	0.2022210	0.0810342	0.0174690	0.2931485
aggression.anger	0.0528586	0.1249831	0.9554577	0.1005087	0.1520969	0.0604562	0.0695452	-0.0275343	0.0657477	0.1146180	0.0611632
aggression.violence	0.0661081	0.2906201	0.5465781	0.1746469	0.1326751	0.0623793	0.0564477	0.2158469	-0.0436690	-0.0161480	-0.0258320
aggression.aggression_social_impact	0.0199923	0.2912773	0.6635470	0.1480428	0.1527398	0.0612080	0.0485477	0.2797050	0.0287037	0.1894996	0.0444737
selfharm.cutting	0.0399613	0.0877897	0.2340288	-0.0368726	0.3146753	0.2450929	0.0672675	0.4197677	0.1298342	0.0982396	-0.0057725
selfharm.hitting	0.0797972	0.0858401	0.1367376	0.0445167	0.8390454	0.0929194	0.0064543	0.0318419	0.1594575	0.1839177	0.1189593
selfharm.banging_head	0.0807096	0.0983643	0.0572073	0.0092898	0.7102043	0.1095340	0.0749824	0.0861172	0.0622817	0.0834091	0.0316940
selfharm.throwing_self	0.0449241	0.1546198	0.1532955	0.0758152	0.5785241	0.0367246	0.2636664	0.1271626	-0.0926529	-0.1439024	-0.0427580
selfharm.self_harm_distressing	0.1064328	0.0671795	0.3480908	0.0962328	0.3101966	0.1344785	0.1155804	0.6190053	0.0372422	0.3273024	0.0738414
eating_GI.eatnorm	0.0403232	0.1350088	0.0722995	0.7802575	0.0716180	0.2193817	-0.0071309	-0.0537625	0.1281635	0.0888874	0.0522333
eating_GI.eat_impact	0.0264519	0.1603731	0.1436861	0.7767861	-0.0006521	0.0813644	0.1240521	0.0083003	0.0056154	0.1118477	0.0158114
eating_GI.constipated	0.0796142	0.0645222	0.1765971	0.1482022	-0.0069866	0.0723587	0.0922520	0.0378867	-0.0410081	0.3774085	0.0243725
eating_GI.GI_distress	0.0473416	0.0822622	0.0445915	0.1934545	0.2245463	0.1958065	0.2322892	0.1143314	0.0423597	0.3633752	-0.0659286
sleep_impact	0.1206532	0.1246777	0.1821075	0.2781920	-0.0321715	0.1153745	0.0484484	0.2086078	0.0985251	0.0364789	0.0884538

Table 2: Supplementary Table S1

ageyears	sex_male	index_finger_mean	adhd	asd	ID	lang	epilepsy	depression	bipolar	anxiety	affected	dx_brd	digit_ratio_raw	facial_masc_raw	Zdrm	Zflm
41.0849315068493	0	7.07563855421687	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.97341272418814	0.953436011633652	0.469775391823678	0.539841315107178
5.06301369863014	0	4.831	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.948985124194837	1.54328406999365	0.599106935231653	0.498654418374079
15.9095890410959	0	6.8155	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.986312534953596	2.48631305459503	-0.750842601497614	1.64019859636647
19.0356164383562	1	NA	FALSE	FALSE	TRUE	TRUE	FALSE	FALSE	TRUE	FALSE	TRUE	3+	NA	-1.9899080523309	NA	-2.9256021282714
9.96712328767123	0	7.34821174277248	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.931861750277048	1.01328003418098	1.59552234201163	0.266457649470293
12.7013698630137	1	6.44106626506024	TRUE	TRUE	TRUE	FALSE	FALSE	TRUE	FALSE	TRUE	TRUE	3+	0.920733085814485	-0.187821231260723	1.73159497586092	-1.21791774022545
11.9671232876712	1	6.973	TRUE	TRUE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	3+	0.985960813884913	1.8756598870194	-1.0388723526922	0.434870067338832
52.7232876712329	0	7.08706626506024	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	1.00843529446322	-0.948177432705898	-0.801229131760898	-0.761409878463409
34.5123287671233	1	6.735	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.941324291606565	2.63028479049334	0.915942591953724	0.0942988476620877
45.0931506849315	1	7.652	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.944999076814995	3.1184685421177	0.637196039643411	0.418433942948714
15.0575342465753	1	7.8	TRUE	FALSE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	2	0.969362819029974	-2.79752358228359	-0.217455014787433	-3.35714902648995
4.98082191780822	1	5.26011830639531	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.900234555162657	-0.0233323975048846	1.8754847424057	-0.812563491326942
33.4219178082192	1	4.40103012048193	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.967736046395609	1.10317951304349	-0.196043035313841	-1.29542849990798
9.63013698630137	1	5.549	FALSE	TRUE	TRUE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	3+	0.993223703584118	-2.00765528510858	-1.41614295394516	-2.54736149055488
4.32876712328767	0	5.78165813253012	FALSE	FALSE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.99356012702766	1.29450410538147	-1.52201275783408	0.232758280169612
11.3561643835616	1	6.61525	FALSE	FALSE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	1	0.994326652368434	0.916577163783636	-1.40605338853687	-0.296632037057392
2.22191780821918	1	4.5705	FALSE	TRUE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	TRUE	2	0.937308203425554	3.20053037023437	0.320830222518341	1.90331412394252
45.0602739726027	1	7.1415	FALSE	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	1.00452127666837	2.99772741185312	-1.80998743214939	0.279683260166662
3.56986301369863	0	4.83370448894743	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.949599399567691	-0.341477757819007	0.51173480222564	-1.32171425843539
4.6958904109589	1	NA	FALSE	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	1	NA	3.29069732811646	NA	1.8719938618348
33.4219178082192	0	NA	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	TRUE	FALSE	2	NA	0.996410987129674	NA	0.623999202502293
48.3342465753425	0	7.026	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	1.01603615121514	-1.25069440989456	-1.19276799872211	-0.888698224965235
7.85205479452055	1	6.31273485337791	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.936211262080358	2.46809236559897	0.746164193781746	1.07434578023898
7.37808219178082	0	NA	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	NA	2.00883862935028	NA	1.01850377217185
52.2684931506849	1	7.3	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	FALSE	0	0.95349062169953	2.96588593749119	0.300637300236753	0.220136801084321
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

ageyears	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6	Factor7	Factor8	Factor9	Factor10	Factor11
41.0849315068493	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
5.06301369863014	0.74794643179529	0.665669421534571	-0.870063379520946	0.210091885909834	-0.109073522445655	1.16837748280975	0.449868235805823	-0.477221284657069	-0.194070086841541	-0.158950331520898	-0.107665405553604
15.9095890410959	0.563010712917452	-1.7142140467899	1.60503931115742	-1.14372806208396	1.27682055553998	-0.337218807248497	0.501624586481267	1.64305131009462	1.38022709914793	0.158208107094537	0.804315512775778
19.0356164383562	0.746629226403026	-0.68945911056888	2.06656828666606	-0.896443219863074	-0.522133128146468	-0.764829496205654	-0.361602012703098	-0.877113921067531	0.829260094474239	-1.35805352797041	-0.855452976089128
9.96712328767123	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
12.7013698630137	-0.50472715325401	0.35999369323113	-1.07077792366996	0.500151565221687	1.16443045754248	0.24910108883881	0.35357799356032	2.72823328088742	-0.750882631917685	1.50132327324671	1.42795636318665
11.9671232876712	0.235631969738386	0.922412555766098	1.52673030432309	0.155859417603592	-0.0656681027574641	-0.229428850922798	-0.332918614003887	-1.07142629087257	0.319498093508234	-0.275540597921467	-0.00608693624367651
52.7232876712329	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
34.5123287671233	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
45.0931506849315	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
15.0575342465753	0.273084934212572	-0.128896859349288	-0.446762486047632	-0.751151751572259	-0.519584746766638	-1.27825862453032	-0.401500339476722	-0.0408698739342565	0.356441528690258	0.704476505266229	-0.761845274548114
4.98082191780822	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
33.4219178082192	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
9.63013698630137	0.749942930357023	0.22246365176742	-0.724165110968692	1.01525682648325	-0.686793349713914	1.41076746743627	0.0153962997714685	-0.435977218547416	-0.30787365205358	-0.449164997650758	-0.35138293171344
4.32876712328767	-0.147688686071538	0.532464923935945	-0.4036600246582	-0.636234699565456	-0.412330596947784	-1.16333365414781	-0.857749783939987	0.144728553094064	-0.916227374962302	-0.262642036745938	0.844951212412659
11.3561643835616	0.208608987459305	-0.970579166650667	-0.382822616917866	-0.774547636088409	-0.37663122770295	0.188053666802665	-0.383523848577554	-0.240498698288248	-1.1358833219222	0.854167766835362	-0.567915888530976
2.22191780821918	0.493547469194733	-0.889237018074268	-0.463993293526893	0.404322656996703	-0.74967321167227	1.25111882120996	-0.703781372617959	3.80941008214173	1.19294400225508	0.441917022530338	-1.02444301250718
45.0602739726027	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
3.56986301369863	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
4.6958904109589	-1.20912289729191	-0.405329795584431	-0.515378199456706	0.0231968515487083	-0.643241700939166	1.39144547537222	-0.421978166245403	-0.0593505034797904	0.771830543363825	-0.586532347379016	0.56330200739529
33.4219178082192	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
48.3342465753425	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7.85205479452055	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7.37808219178082	-1.93570155997193	0.398214534236872	-0.536840532450188	-0.638116306077571	-0.339689835951671	-0.562532594682659	0.739265330610972	0.311368894101221	1.19224635748094	-0.722919579076933	0.719405667974506
52.2684931506849	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
...	...	...	...	...	...	...	...	...	...	...	...

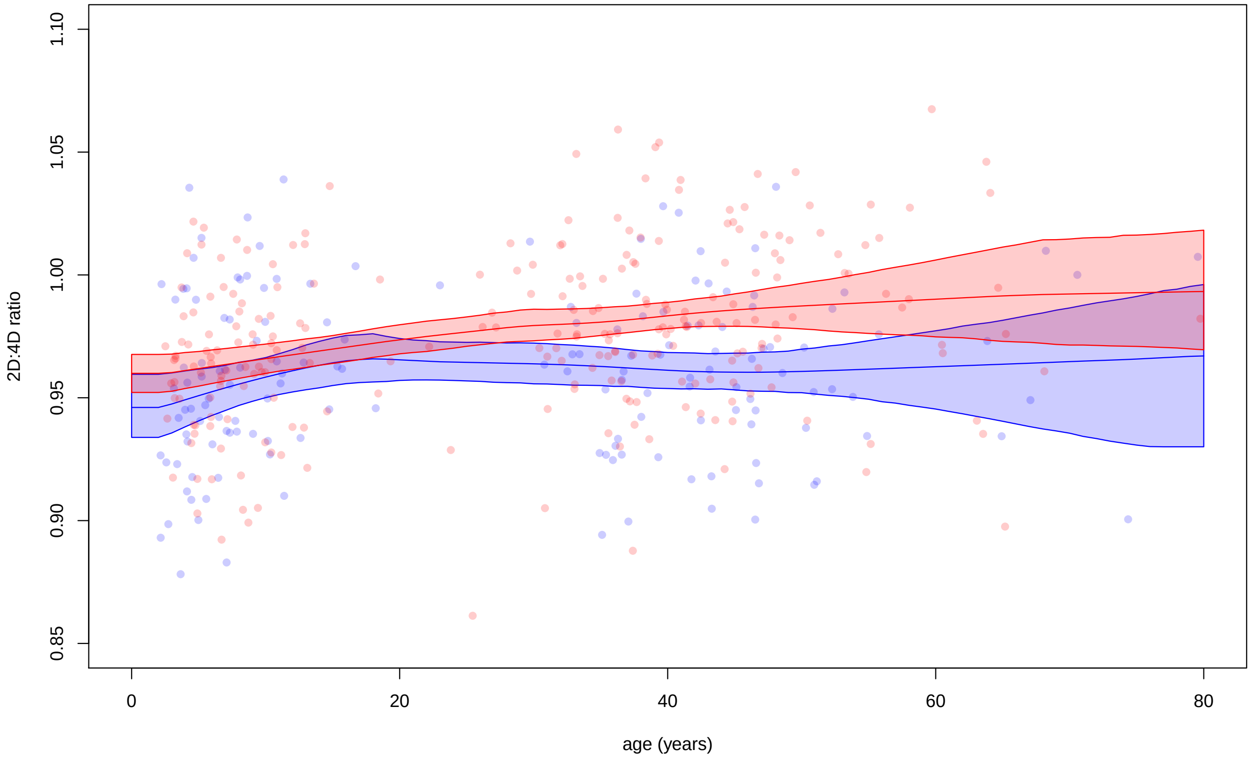
ageyears	PC1	PC2	PC3	PC4	PC5	UKBB_testosterone.p0.01	morePRSes
41.0849315068493	NA	NA	NA	NA	NA	NA	...
5.06301369863014	4.68806426397683	-4.41687861785199	0.997208892612168	7.61791784934	6.20459958000375	2	...
15.9095890410959	-6.10069572527619	3.68271060938101	6.81724862835369	3.80656741128771	-3.67835200411538	2	...
19.0356164383562	NA	NA	NA	NA	NA	NA	...
9.96712328767123	NA	NA	NA	NA	NA	NA	...
12.7013698630137	-5.85607919435734	-2.78379802226688	-6.66298051659031	4.61501331499839	1.9171931994545	2	...
11.9671232876712	-8.4946334050943	-3.67149754617962	-5.06938468118347	-2.6375318494995	-2.02700185187395	1	...
52.7232876712329	NA	NA	NA	NA	NA	NA	...
34.5123287671233	NA	NA	NA	NA	NA	NA	...
45.0931506849315	NA	NA	NA	NA	NA	NA	...
15.0575342465753	0.0815510600689723	9.80800295947389	-0.734077427633593	-2.37810924780002	3.88390694436289	1	...
4.98082191780822	NA	NA	NA	NA	NA	NA	...
33.4219178082192	NA	NA	NA	NA	NA	NA	...
9.63013698630137	NA	NA	NA	NA	NA	NA	...
4.32876712328767	9.15413754411236	9.73204544123858	1.8353418883636	-3.85085851966184	-5.63114736309893	1	...
11.3561643835616	-2.08889695546891	-3.33026964213117	0.727527909419126	3.14353975723333	7.2587523102397	2	...
2.22191780821918	-2.91286286802258	6.48034704148293	7.08055246871024	-7.19693504680407	0.542997546906937	1	...
45.0602739726027	NA	NA	NA	NA	NA	NA	...
3.56986301369863	NA	NA	NA	NA	NA	NA	...
4.6958904109589	NA	NA	NA	NA	NA	NA	...
33.4219178082192	NA	NA	NA	NA	NA	NA	...
48.3342465753425	NA	NA	NA	NA	NA	NA	...
7.85205479452055	NA	NA	NA	NA	NA	NA	...
7.37808219178082	NA	NA	NA	NA	NA	NA	...
52.2684931506849	NA	NA	NA	NA	NA	NA	...
...	...	...	...	...	...	...	...

Figure 2: facial and digital masculinity by age

```
### lboot() returns the lowess trend of the
### data as well as its 95% CI; the object returned by lboot()
### can be visualized using plotl() as shown below

set.seed(1283)
### get the trends for TD males
idx = !dat$affected & dat$sex_male==1
tdM_flm = lboot(dat$ageyears,dat$facial_masc_raw,subset=idx,return.boot=T)
tdM_drm = lboot(dat$ageyears,dat$digit_ratio_raw,subset=idx,return.boot=T)

### get the trends for TD females
idx = !dat$affected & dat$sex_male==0
tdF_flm = lboot(dat$ageyears,dat$facial_masc_raw,subset=idx,return.boot=T)
tdF_drm = lboot(dat$ageyears,dat$digit_ratio_raw,subset=idx,return.boot=T)

set.seed(7751)
### get the trends for affected males
idx = dat$affected & dat$sex_male==1
affM_flm = lboot(dat$ageyears,dat$facial_masc_raw,subset=idx,return.boot=T)
affM_drm = lboot(dat$ageyears,dat$digit_ratio_raw,subset=idx,return.boot=T)

### get the trends for affected females
idx = dat$affected & dat$sex_male==0
affF_flm = lboot(dat$ageyears,dat$facial_masc_raw,subset=idx,return.boot=T)
affF_drm = lboot(dat$ageyears,dat$digit_ratio_raw,subset=idx,return.boot=T)
```

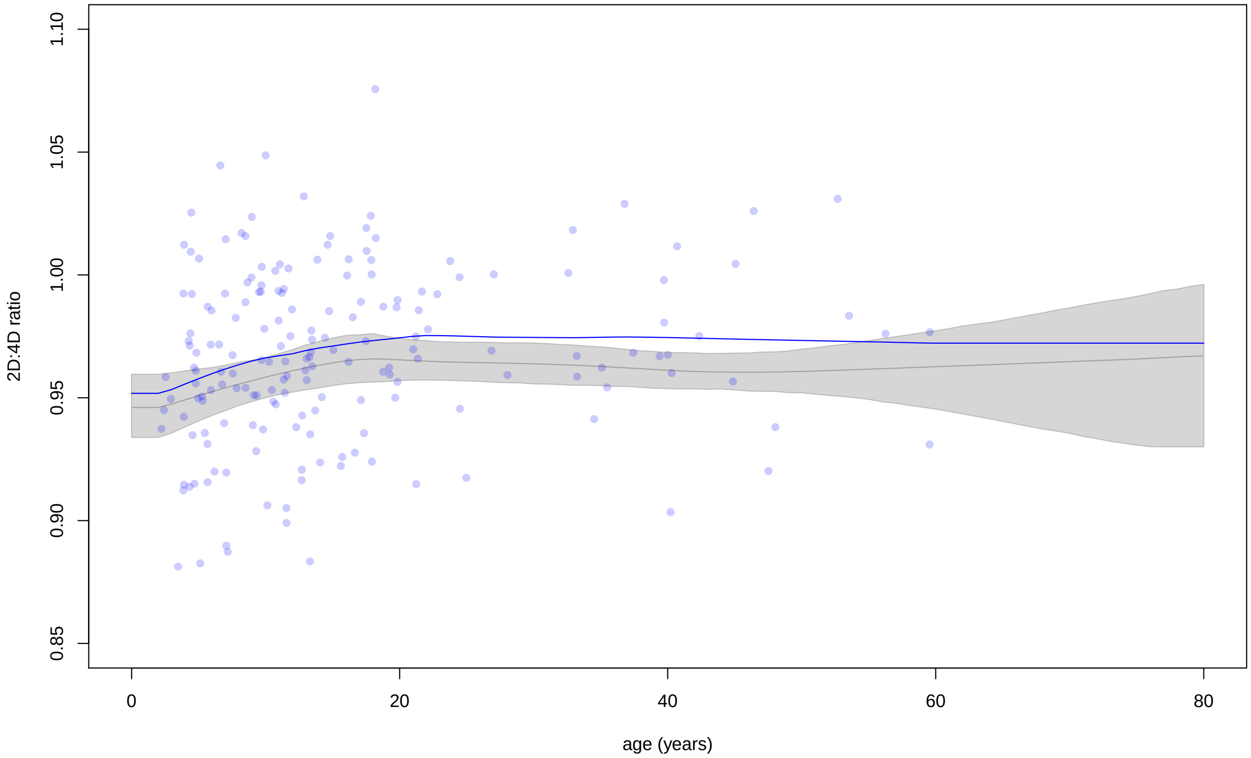
TD male and female trends for digit ratio

```
plotl(tdM_drm,l.col="blue",shade.col=rgb(0,0,1,0.2),pt.col=rgb(0,0,1,0.2),
plot.points=T,ylab="2D:4D ratio",ylim=c(0.85,1.1))
plotl(tdF_drm,l.col="red",shade.col=rgb(1,0,0,0.2),pt.col=rgb(1,0,0,0.2),
plot.points=T,ylab="2D:4D ratio",ylim=c(0.85,1.1),add=T)
```



TD male and AFF male trends for digit ratio

```
plotl(tdM_drm,l.col="grey",shade.col=rgb(0.2,0.2,0.2,0.2),pt.col=rgb(0.2,0.2,0.2,0.2),
plot.points=F,ylab="2D:4D ratio",ylim=c(0.85,1.1))
plotl(affM_drm,l.col="blue",shade.col=rgb(0,0,1,0.2),pt.col=rgb(0,0,1,0.2),
plot.points=T,ylab="2D:4D ratio",ylim=c(0.85,1.1),add=T,plot.ci=F)
```

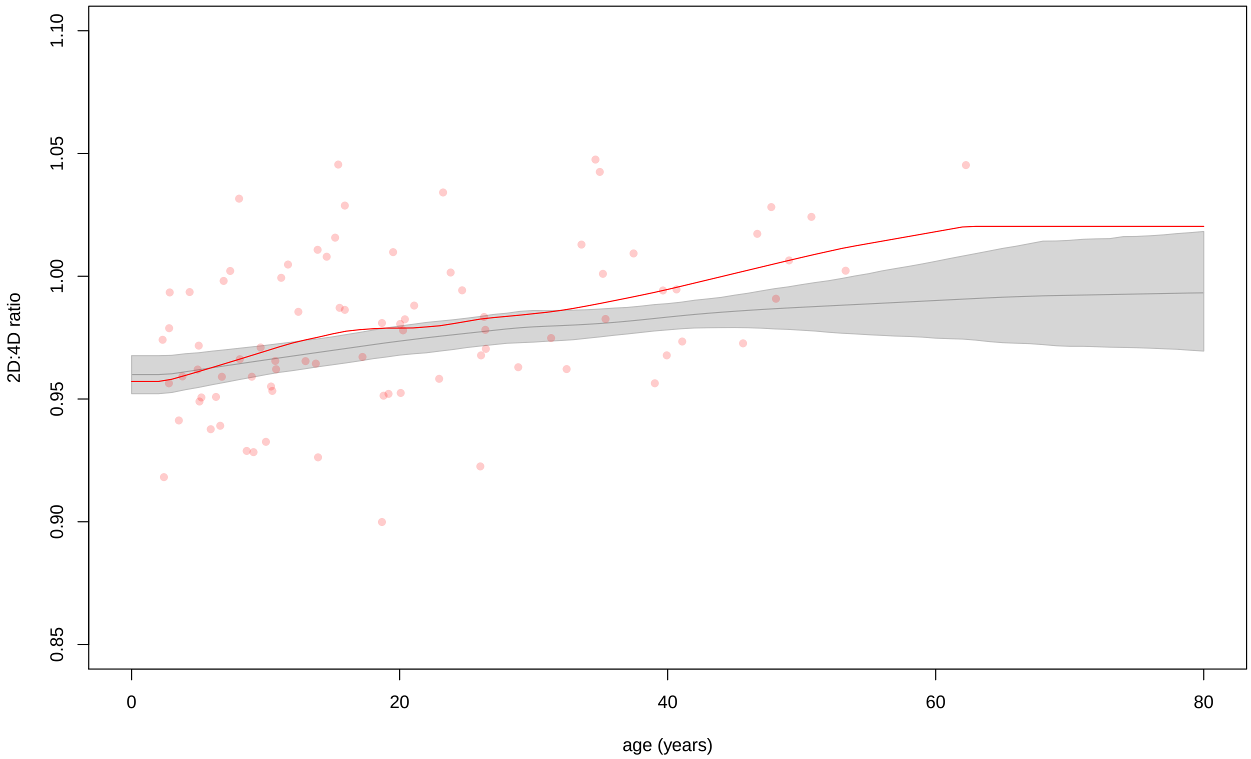



```
### look at the empirical p value for Ha: aff > masc. than TD
### (for digit ratio, lower value is more masculine)
sum(colSums(tdM_drm$b)<sum(affM_drm$y))/1000 ### this is the empirical p-value
```

```
## [1] 0.991
```

TD female and AFF female trends for digit ratio

```
plotl(tdF_drm,l.col="grey",shade.col=rgb(0.2,0.2,0.2,0.2),pt.col=rgb(0.2,0.2,0.2,0.2),
plot.points=F,ylab="2D:4D ratio",ylim=c(0.85,1.1))
plotl(affF_drm,l.col="red",shade.col=rgb(1,0,0,0.2),pt.col=rgb(1,0,0,0.2),
plot.points=T,ylab="2D:4D ratio",ylim=c(0.85,1.1),add=T,plot.ci=F)
```

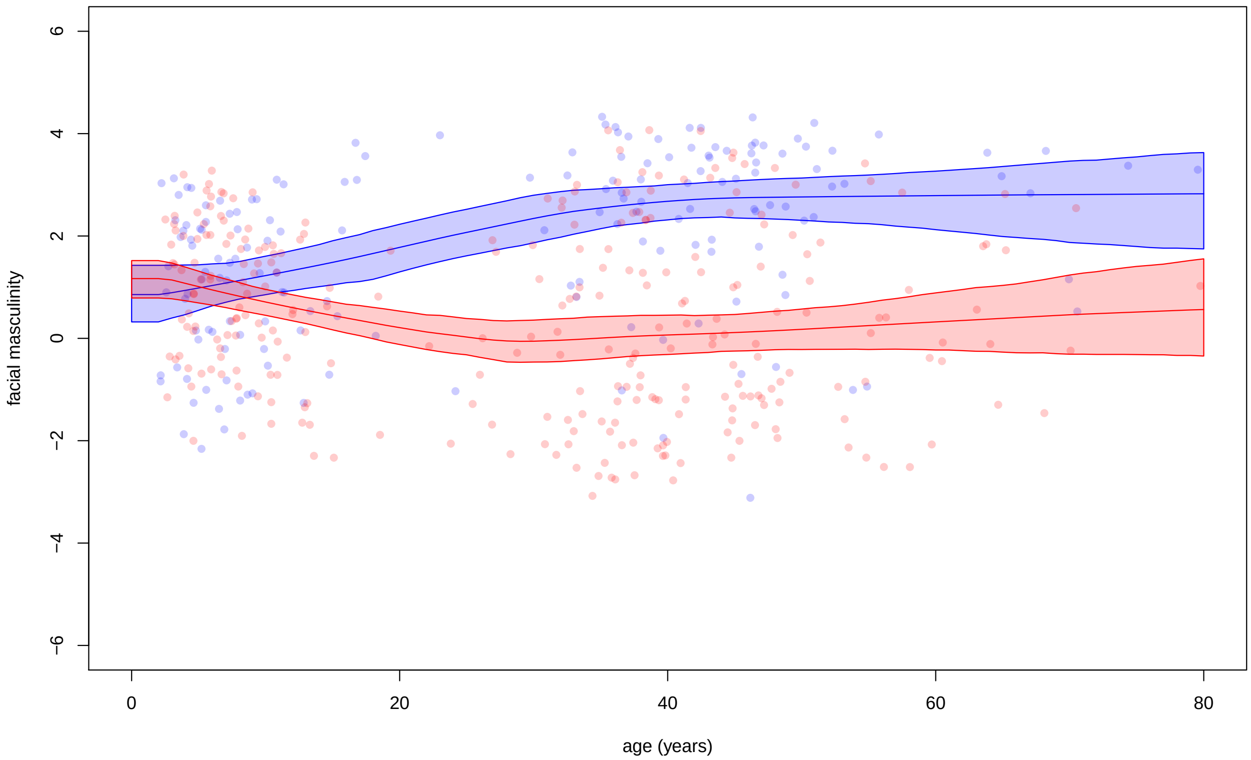



```
### look at the empirical p value for Ha: aff > masc. than TD
### (for digit ratio, lower value is more masculine)
sum(colSums(tdF_drm$b)<sum(affF_drm$y))/1000 ### this is the empirical p-value
```

```
## [1] 1
```

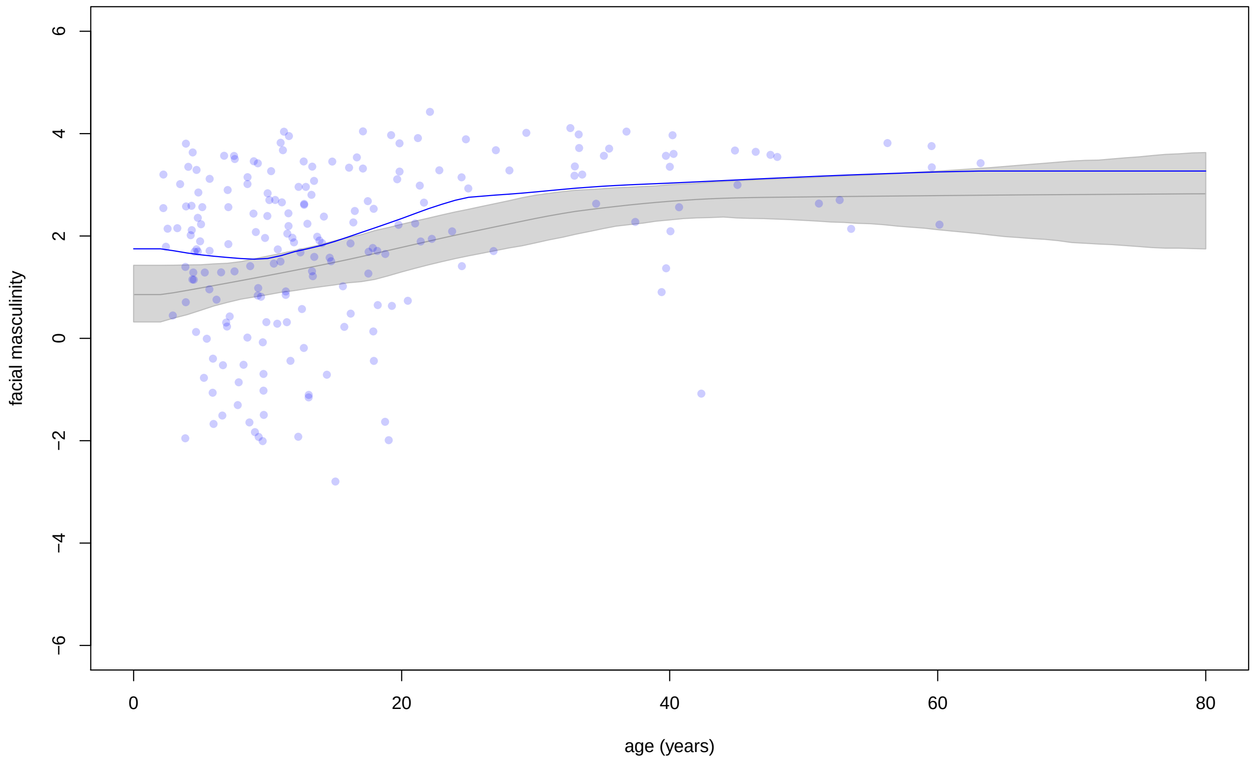
TD male and female trends for facial masculinity

```
plotl(tdM_flm,l.col="blue",shade.col=rgb(0,0,1,0.2),pt.col=rgb(0,0,1,0.2),
plot.points=T,ylab="facial masculinity",ylim=c(-6,6))
plotl(tdF_flm,l.col="red",shade.col=rgb(1,0,0,0.2),pt.col=rgb(1,0,0,0.2),
plot.points=T,ylab="facial masculinity",ylim=c(-6,6),add=T)
```



TD male and AFF male trends for facial masculinity

```
plotl(tdM_flm,l.col="grey",shade.col=rgb(0.2,0.2,0.2,0.2),pt.col=rgb(0.2,0.2,0.2,0.2),
plot.points=F,ylab="facial masculinity",ylim=c(-6,6))
plotl(affM_flm,l.col="blue",shade.col=rgb(0,0,1,0.2),pt.col=rgb(0,0,1,0.2),
plot.points=T,ylab="facial masculinity",ylim=c(-6,6),add=T,plot.ci=F)
```

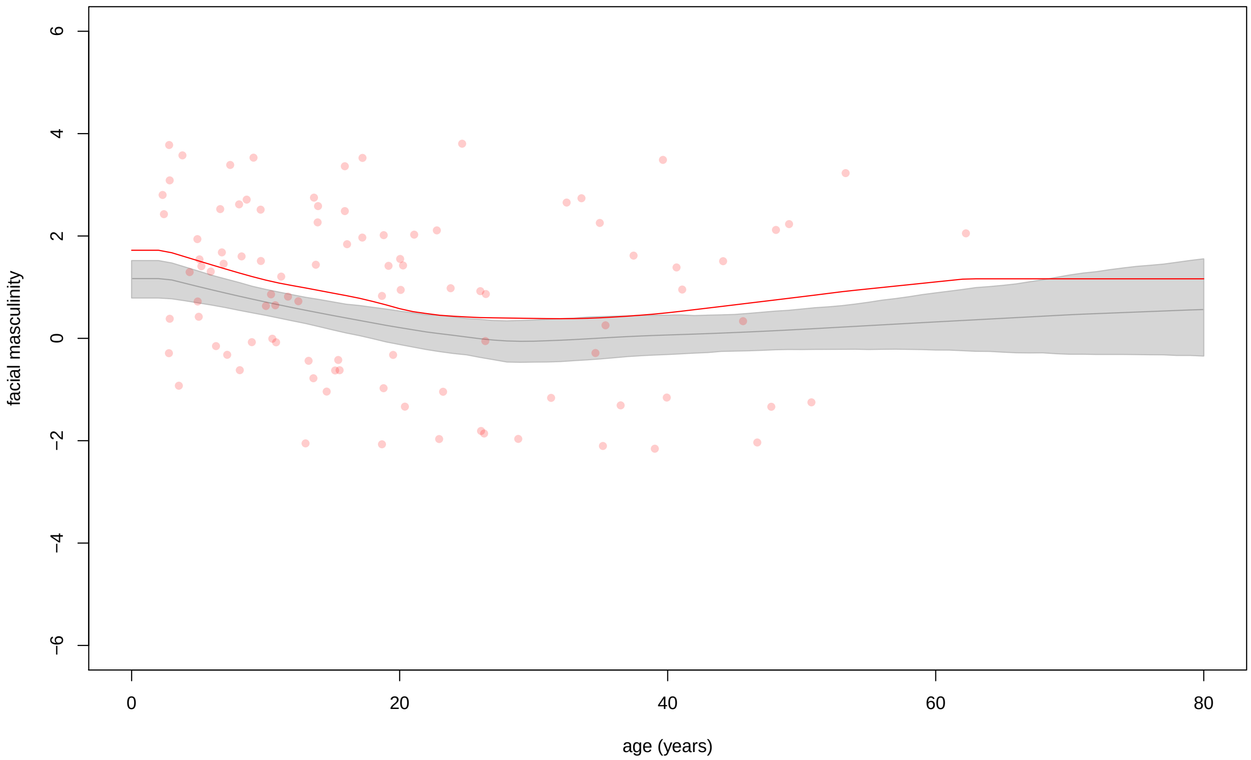



```
### look at the empirical p value for Ha: aff > masc. than TD
sum(colSums(tdM_flm$b)>sum(affM_flm$y))/1000 ### this is the empirical p-value
```

```
## [1] 0.002
```

TD female and AFF female trends for facial masculinity

```r
plotl(tdF_flm,l.col="grey",shade.col=rgb(0.2,0.2,0.2,0.2),pt.col=rgb(0.2,0.2,0.2,0.2),
plot.points=F,ylab="facial masculinity",ylim=c(-6,6))
plotl(affF_flm,l.col="red",shade.col=rgb(1,0,0,0.2),pt.col=rgb(1,0,0,0.2),
plot.points=T,ylab="facial masculinity",ylim=c(-6,6),add=T,plot.ci=F)
```




```r
### look at the empirical p value for Ha: aff > masc. than TD
sum(colSums(tdF_flm$b)>sum(affF_flm$y))/1000 ### this is the empirical p-value
```

```
## [1] 0
```

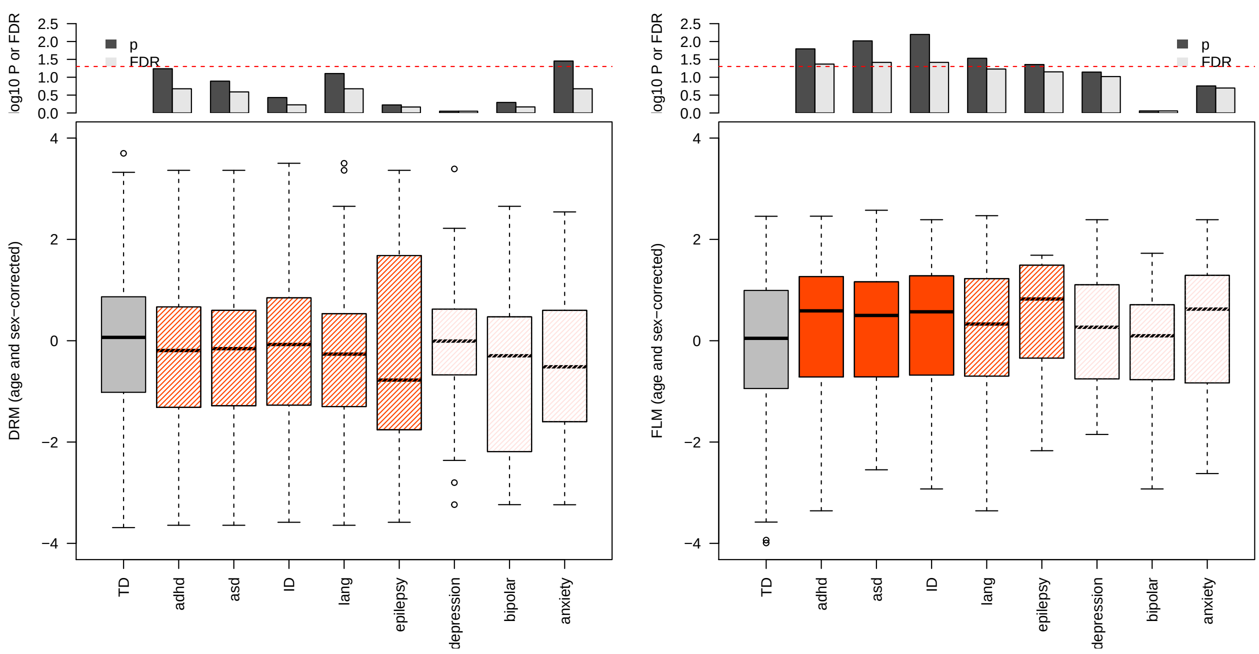
Figure 3: Relationships with diagnosis and parent-reported problems

Top: Boxplots showing masculinity scores distribution and barplots showing significance

```
### pull out the Dx indicators
dxlab = c("adhd","asd","ID","lang","epilepsy","depression","bipolar","anxiety")
dx = as.data.frame(sapply(dat[,dxlab],as.integer))
rownames(dx) = rownames(dat)

cc = c("grey",rep("orangered",5),rep("mistyrose",3))

### structure the masculinity data according to Dx
ll = lapply(dx,function(x) dat$Zdrm[x==1])
ll = c(list(TD=dat$Zdrm[rowSums(dx)==0]),ll)
ll_drm = ll
ll = lapply(dx,function(x) dat$Zflm[x==1])
ll = c(list(TD=dat$Zflm[rowSums(dx)==0]),ll)
ll_flm = ll

## t-tests comparing TD to all other Dxs
td_vs_dx = function(x) {
 p = sapply(x[-1],function(y) t.test(x[[1]],y)$p.v)
 fdr = p.adjust(p,'fdr')
 out = cbind(p,fdr)
 rownames(out) = names(x)[-1]
 return(out)
}

p_drm = td_vs_dx(ll_drm)
p_flm = td_vs_dx(ll_flm)
```

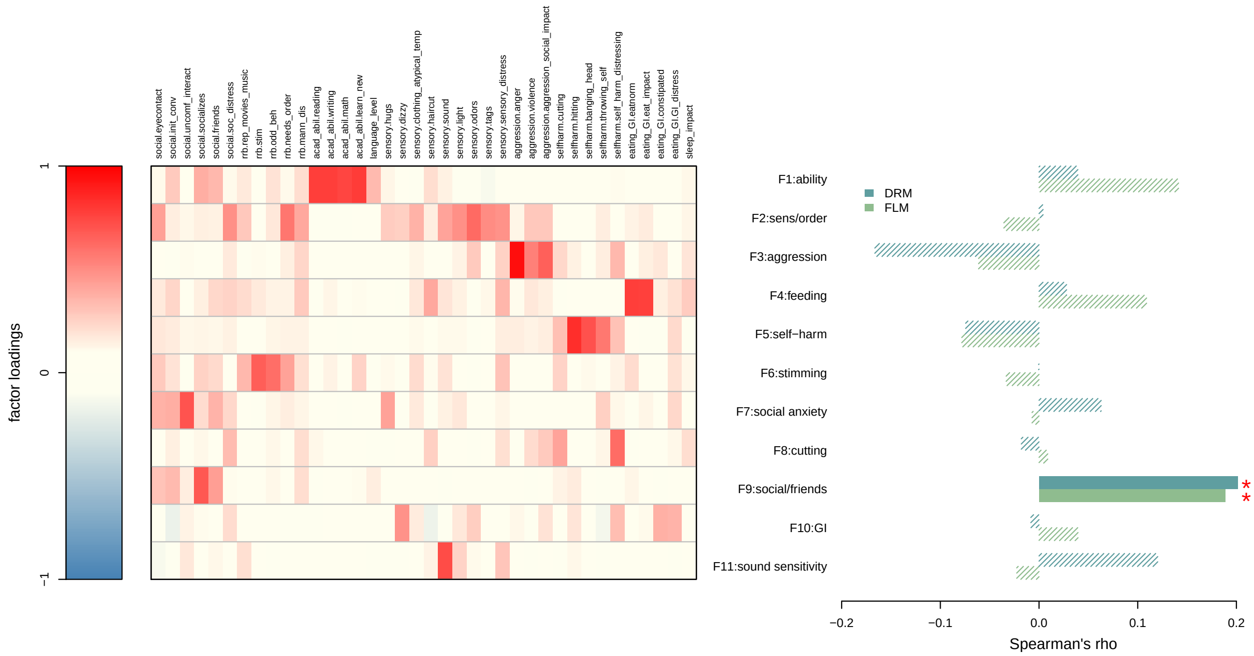
```
layout(matrix(c(1,3,2,4),2,2),heights=c(1,5))
par(mar=c(0,4,1,2))
  barplot(-log10(t(rbind(c(NA,NA),p_drm))),
  beside=T,
  las=2,
  ylim=c(0,2.5),
  ylab="-log10 P or FDR",
  names.arg=rep("",9),
  legend.text=c("p","FDR"),
  args.legend=list(x="topleft",bty="n",border=NA,inset=0.03))
  abline(h=-log10(0.05),col='red',lty=2)
  barplot(-log10(t(rbind(c(NA,NA),p_flm))),
  beside=T,
  las=2,
  ylim=c(0,2.5),
  ylab="-log10 P or FDR",
  names.arg=rep("",9),
  legend.text=c("p","FDR"),
  args.legend=list(x="topright",bty="n",border=NA,inset=0.03))
```

```r
  abline(h=-log10(0.05),col='red',lty=2)

## the boxplots showing the distribution of the masculinity scores within
par(mar=c(5,4,0.5,2))
  bp = boxplot(ll_drm,las=2,ylim=c(-4,4),
  col=c("grey",rep("white",8)),
  ylab="DRM (age and sex-corrected)",
  xaxs="i")
  ### pattern fills to emphasize (non)significance
  rect((2:9)-.4,
  bp$stats[2,-1],
  (2:9)+.4,
  bp$stats[4,-1],
  density=c(rep(30,8)), ## tweaked according to which comparisons are sig.
  col=cc[-1],border="black")
  bp = boxplot(ll_flm,las=2,ylim=c(-4,4),
  col=c("grey",rep("orangered",3),rep("white",5)),
  ylab="FLM (age and sex-corrected)",
  xaxs="i")
  ### pattern fills to emphasize (non)significance
  rect((2:9)-.4,
  bp$stats[2,-1],
  (2:9)+.4,
  bp$stats[4,-1],
  density=c(0,0,0,rep(30,6)), ## tweaked according to which comparisons are sig.
  col=cc[-1],border="black")
```



Bottom: Parent-report Factors

```
# Xs is the matrix of parent-reported items (we are only distributing factor scores)
# fac = factanal(scale(Xs),factors=11,scores="regression")

### grab the factor scores from the supplemental table
S =  dat[,grep("Factor",colnames(dat))]
### look at the correlations
cors = cor(dat[,c("Zdrm","Zflm")],S,use="pairwise.complete.obs",method="spearman")

 ### set layout
 layout(matrix(c(1,2,3),1,3),widths=c(1.5,5,5))
 ### set colors, labels, and breaks for loadings
 cp = colorRampPalette(c("steelblue","ivory","red"))
 flab = c("F1:ability","F2:sens/order","F3:aggression","F4:feeding",
    "F5:self-harm","F6:stimming","F7:social anxiety","F8:cutting",
    "F9:social/friends","F10:GI","F11:sound sensitivity")
 bk = c(-1,seq(-1,-0.1,length.out=127),0,seq(0.1,1,length.out=127),1)

 ### the key for the factor loadings
 par(mar=c(5,7,12,1))
 img(as.matrix(seq(1,-1,length.out=256)),col=cp(256),breaks=bk)
 axis(2,at=c(0,256/2,256),labels=c(1,0,-1))
 mtext("factor loadings",side=2,at=256/0,line=3,cex=0.8)

 ### the factor loadings
 par(mar=c(5,1,12,1))
 img(t(l),breaks=bk,col=cp(256))
 mtext(rownames(l),side=3,at=c(1:nrow(l))-0.5,las=2,line=0.5,cex=0.5)
 abline(h=c(0:12),col='grey')
 box()

 ### the barplot of correlations w/ factor scores
 par(mar=c(5,9,12,2))
 bp = barplot(cors[2:1,11:1],beside=T,las=2,yaxs="i",names.arg=flab[11:1],axes=F,
    ylab="",col=c("darkseagreen","cadetblue"),
    legend.text=c("FLM","DRM"),
    args.legend=list(x="topleft",inset=0.03,border=NA,bty='n',density=-1),
    border=NA,xlim=c(-0.2,0.22),
    density=rev(c(rep(30,16),-1,-1,rep(30,4))),horiz=T)
 axis(1,line=1.5)
 mtext("Spearman's rho",side=1,at=0.025,line=4,cex=0.8)
 text(c(0.21,0.21),bp[1:2,3],rep("*",2),col='red',cex=2)
```



factor loadings
1
0
−1
social.eyecontact
social.init_conv
social.uncomf_interact
social.socializes
social.friends
social.soc_distress
rrb.rep_movies_music
rrb.stim
rrb.odd_beh
rrb.needs_order
rrb.mann_dis
acad_abil.reading
acad_abil.writing
acad_abil.math
acad_abil.learn_new
language_level
sensory.hugs
sensory.dizzy
sensory.clothing_atypical_temp
sensory.haircut
sensory.sound
sensory.light
sensory.odors
sensory.tags
sensory.sensory_distress
aggression.anger
aggression.violence
aggression.aggression_social_impact
selfharm.cutting
selfharm.hitting
selfharm.banging_head
selfharm.throwing_self
selfharm.self_harm_distressing
eating_GI.eatnorm
eating_GI.eat_impact
eating_GI.constipated
eating_GI.GI_distress
sleep_impact
F1:ability
F2:sens/order
F3:aggression
F4:feeding
F5:self−harm
F6:stimming
F7:social anxiety
F8:cutting
F9:social/friends
F10:GI
F11:sound sensitivity
DRM
FLM
*
*
−0.2
−0.1
0.0
0.1
0.2
Spearman's rho

Bottom: Statistics

Table 3: Digit Ratio Masculinity

Factor	ρ	FDR
Factor1	0.0393443	0.9946875
Factor2	0.0041213	0.9946875
Factor3	-0.1663960	0.0976235
Factor4	0.0279256	0.9946875
Factor5	-0.0743621	0.8014244
Factor6	-0.0004705	0.9946875
Factor7	0.0629893	0.8176376
Factor8	-0.0179701	0.9946875
Factor9	**0.2012962**	**0.0444052**
Factor10	-0.0083417	0.9946875
Factor11	0.1202564	0.3206328

Table 4: Facial Landmark Masculinity

Factor	ρ	FDR
Factor1	0.1413869	0.1648585
Factor2	-0.0356959	0.8390477
Factor3	-0.0612753	0.7664615
Factor4	0.1089886	0.3476934
Factor5	-0.0783222	0.6338121
Factor6	-0.0333277	0.8390477
Factor7	-0.0071165	0.9133422
Factor8	0.0088366	0.9133422
Factor9	**0.1886747**	**0.0403774**
Factor10	0.0394948	0.8390477
Factor11	-0.0226260	0.8913875

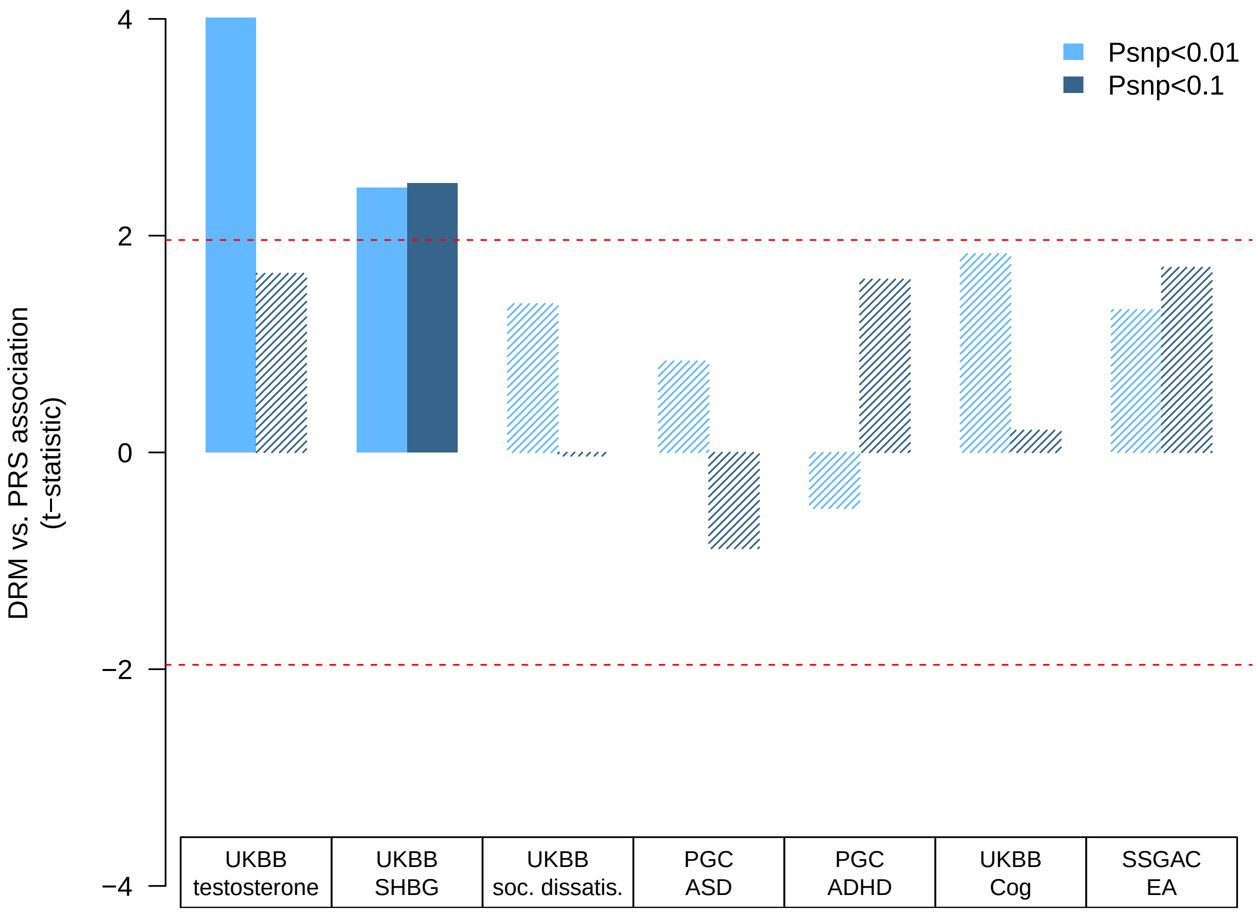
Figure 4: PRS in devGenes

Left: PRS Associations

```
### pull out the PRS and covariates from the main table for convenience
prs = dat[,grep("p0",colnames(dat))]
covars = dat[,c(2:3,grep("PC",colnames(dat)))]
covars[[1]] = log(covars[[1]])

### wrapper to grab the PRS-related effect (x) and associated statistics
### from a linear model
fsig = function(x,y) summary(lm(y~.,data=data.frame(covars,x)))$coef[9,]

cfsoc = t(apply(prs,2,fsig,S[,9]))
cfdrm = t(apply(prs,2,fsig,dat$Zdrm))
cfflm = t(apply(prs,2,fsig,dat$Zflm))

### add FDR
cfsoc = cbind(cfsoc,FDR = p.adjust(cfsoc[,4],'fdr'))
cfdrm = cbind(cfdrm,FDR = p.adjust(cfdrm[,4],'fdr'))
cfflm = cbind(cfflm,FDR = p.adjust(cfflm[,4],'fdr'))

### assemble the t-statistics and arrange for the barplot
p1 = cbind(drm=cfdrm[grepl("0\\.1$",rownames(cfdrm)),3],
    flm=cfflm[grepl("0\\.1$",rownames(cfflm)),3],
    F9=cfsoc[grepl("0\\.1$",rownames(cfsoc)),3])
p01 = cbind(drm=cfdrm[grepl("0\\.01$",rownames(cfdrm)),3],
    flm=cfflm[grepl("0\\.01$",rownames(cfflm)),3],
    F9=cfsoc[grepl("0\\.01$",rownames(cfsoc)),3])

### this is what will be plotted
pdrm = cbind(p01[,1],p1[,1])
pflm = cbind(p01[,2],p1[,2])
psoc = cbind(p01[,3],p1[,3])

### helper function to pattern fill according to significance
fdens = function(x) ifelse(t(abs(x)>=1.96),-1,30)
### define colors and labels
cc = c("steelblue1","steelblue4")
plab = c("UKBB\ntestosterone","UKBB\nSHBG","UKBB\nsoc. dissatis.","PGC\nASD","PGC\nADHD","UKBB\nCog","S
```

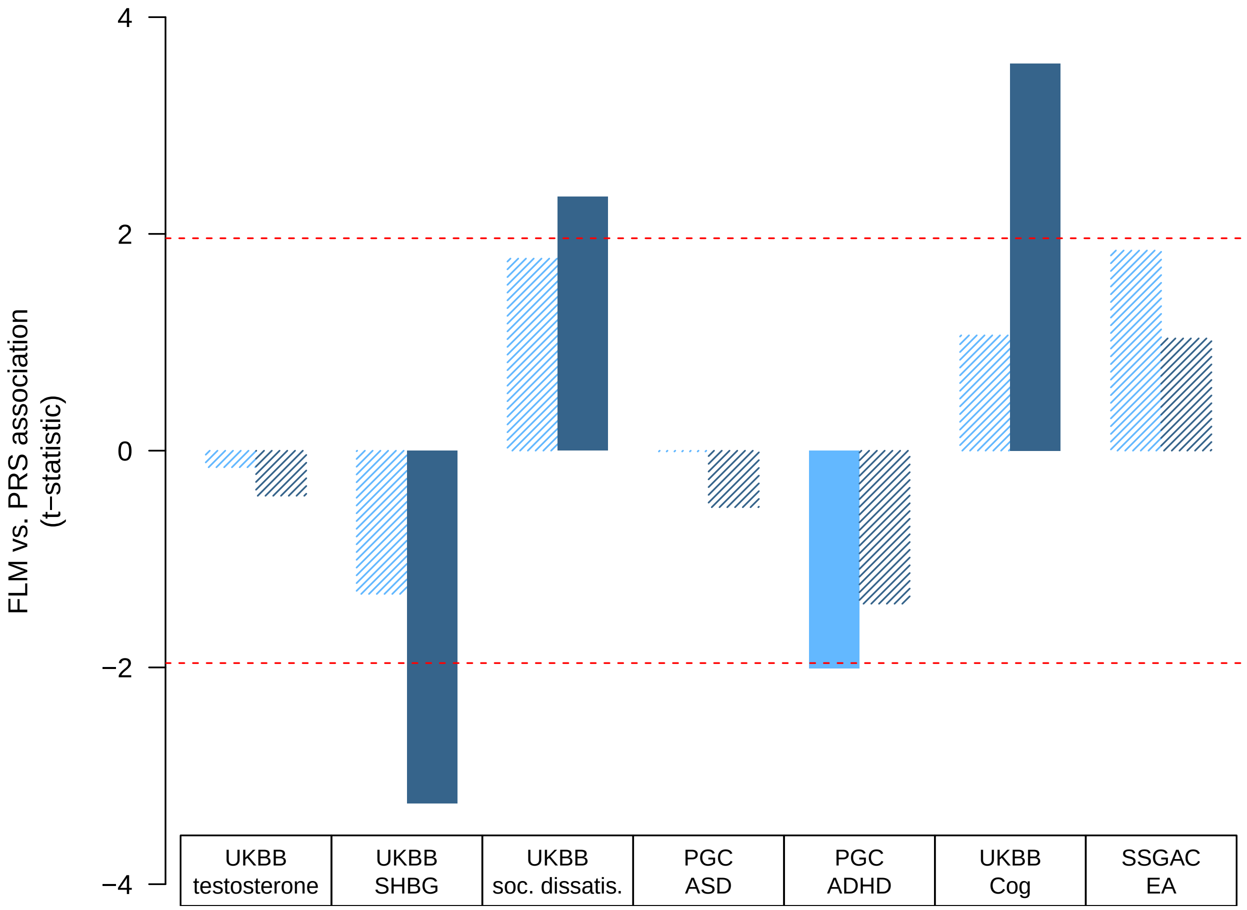
Digit Ratio Masculinity

```
par(mar=c(1,5,2,2))
bp = barplot(t(pdrm),
  beside=T,
  las=2,
  ylim=c(-4.2,4),
  names.arg=rep("",7),
  density=fdens(pdrm),
  col=cc,border=NA,
  legend.text=c("Psnp<0.01","Psnp<0.1"),
  args.legend=list(x="topright",bty='n',border=NA,density=-1),
  ylab="DRM vs. PRS association\n(t-statistic)")
  rect(t(bp)[,1]-1,-4.20,t(bp)[,2]+1,-3.55)
  text(bp[1,]+0.5,rep(-3.88,7),plab,cex=0.85)
  abline(h=c(-1.96,1.96),col='red',lty=2)
```



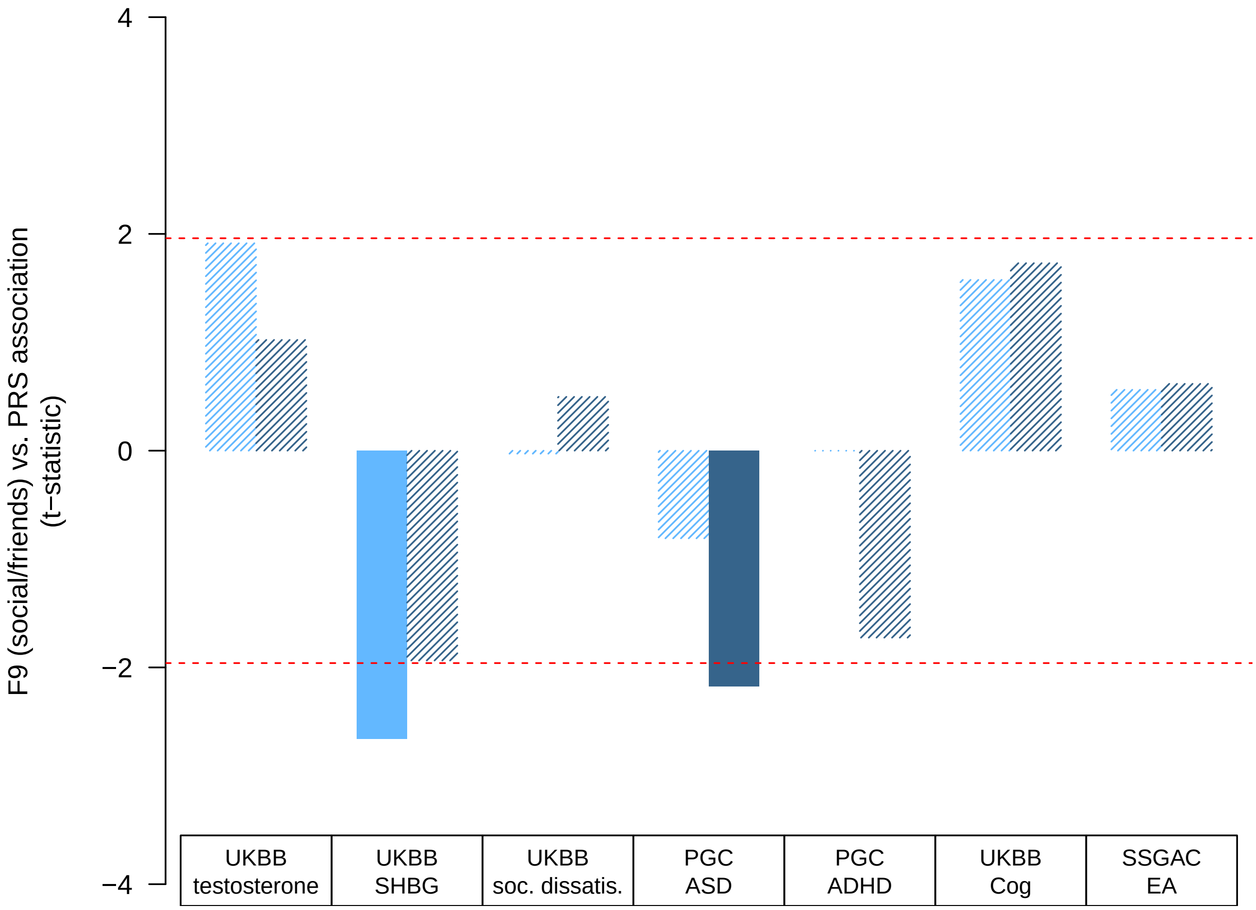
Facial Landmark Masculinity

```
par(mar=c(1,5,2,2))
barplot(t(pflm),
  beside=T,
  las=2,
  ylim=c(-4.2,4),
  names.arg=rep("",7),
  density=fdens(pflm),
  col=cc,border=NA,
  ylab="FLM vs. PRS association\n(t-statistic)")
  abline(h=c(-1.96,1.96),col='red',lty=2)
  rect(t(bp)[,1]-1,-4.20,t(bp)[,2]+1,-3.55)
  text(bp[1,]+0.5,rep(-3.88,7),plab,cex=0.85)
```



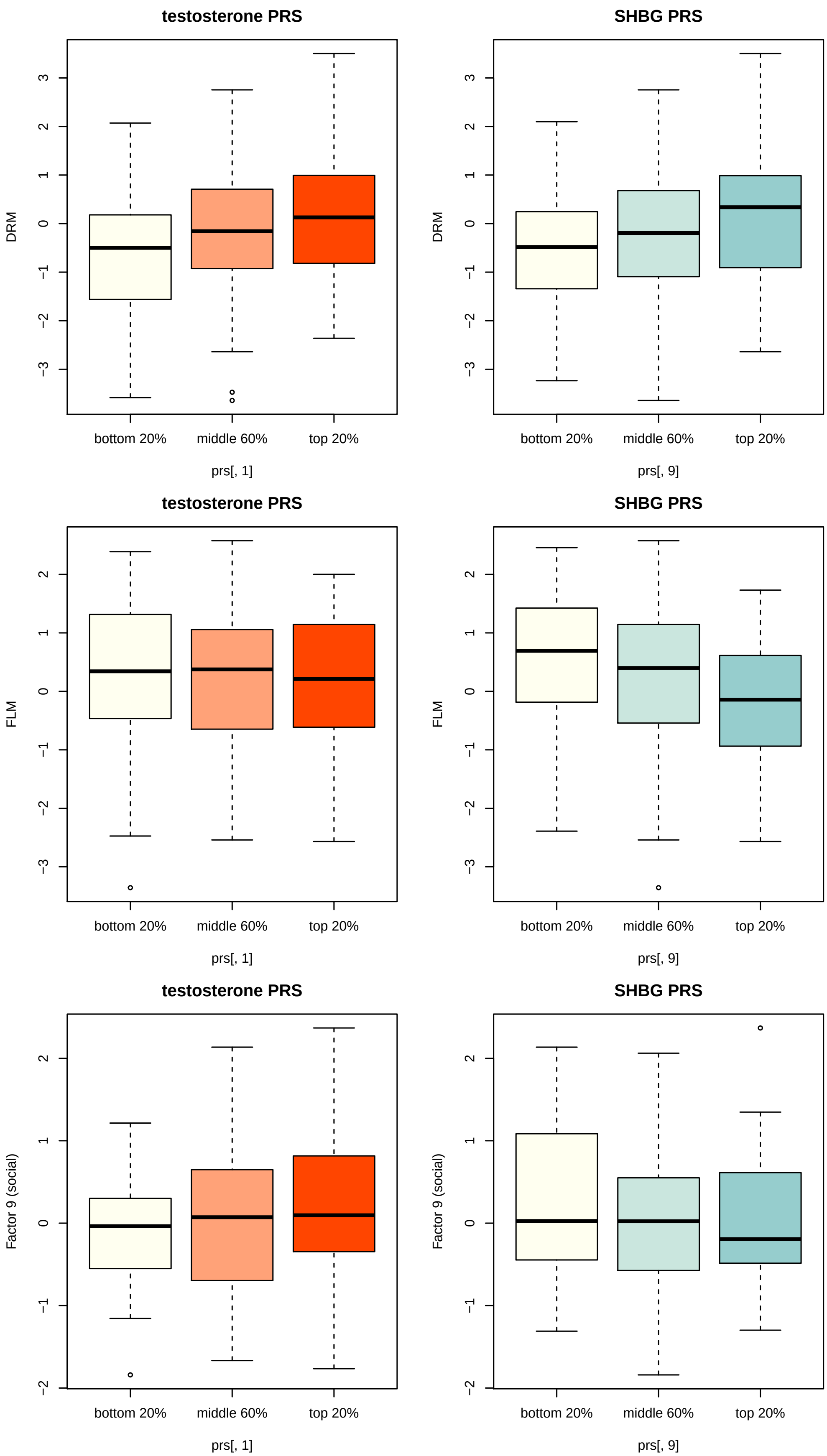
Factor 9 (social)

```
par(mar=c(1,5,2,2))
barplot(t(psoc),
  beside=T,
  las=2,
  ylim=c(-4.2,4),
  names.arg=rep("",7),
  density=fdens(psoc),
  col=cc,border=NA,
  ylab="F9 (social/friends) vs. PRS association\n(t-statistic)")
  abline(h=c(-1.96,1.96),col='red',lty=2)
  rect(t(bp)[,1]-1,-4.20,t(bp)[,2]+1,-3.55)
  text(bp[1,]+0.5,rep(-3.88,7),plab,cex=0.85)
```



Right: Categorical PRS Comparison

```
## set up colors, layout, and labels
par(mfrow=c(3,2),mar=c(4,4,3,2))
cc1 = colorRampPalette(c("ivory","orangered1"))(3)
cc2 = colorRampPalette(c("ivory","paleturquoise3"))(3)
nn = c("bottom 20%","middle 60%","top 20%")

 boxplot(dat$Zdrm~prs[,1],
    names=nn,
    ylab="DRM",
    main="testosterone PRS",
    col=cc1)
 boxplot(dat$Zdrm~prs[,9],
    names=nn,
    ylab="DRM",
    main="SHBG PRS",
    col=cc2)
 boxplot(dat$Zflm~prs[,1],
    names=nn,
    ylab="FLM",
    main="testosterone PRS",
    col=cc1)
 boxplot(dat$Zflm~prs[,9],
    names=nn,
    ylab="FLM",
    main="SHBG PRS",
    col=cc2)
 boxplot(S[,9]~prs[,1],
    names=nn,
    ylab="Factor 9 (social)",
    main="testosterone PRS",
    col=cc1)
 boxplot(S[,9]~prs[,9],
    names=nn,
    ylab="Factor 9 (social)",
    main="SHBG PRS",
    col=cc2)
```


testosterone PRS
SHBG PRS
DRM
FLM
Factor 9 (social)
bottom 20%
middle 60%
top 20%
prs[, 1]
prs[, 9]
−3
−2
−1
0
1
2
3