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Supplementary Materials for

A randomized placebo-controlled pilot trial shows that intranasal vasopressin improves social deficits in children with autism

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Table S1. Raw data and SAS code for the data and analyses shown in Table 1.

```
DATA SI1; INPUT  Drug_Status &$16. Sex &$16. EthnicityForAnalysis &$16. Age
SB5_FSIQ_Standard_Score V1V2_SRS2T_Total_Score V1_CGI_Social_Interaction_and_Co
V1_AVP_level_pg_mL_ V1_AVPR1a_OXTR; Lines;
Placebo  Male  Other  8.525081217  68  80  5  1.037  3.085927963
Active  Male  Caucasian  6.343193349  70  81.5  5  0.598  1.885335923
Placebo  Female  Caucasian  12.90243101  98  88  4  0.514  4.152868271
Placebo  Male  Caucasian  8.327744013  118  90  5  2.085  1.085920333
Active  Male  Other  12.99551029  58  71  5  0.869  4.076757431
Placebo  Male  Caucasian  11.93878668  74  78.5  5  2.209  2.30529213
Active  Female  Caucasian  6.184296978  88  81  5  4.028  0.052930832
Active  Male  Caucasian  6.652545079  66  81  5  2.922  2.47912407
Placebo  Male  Caucasian  11.69251442  99  90  4  1.811  1.979845047
Active  Male  Caucasian  10.86016207  78  66.5  4  1.148  2.046735764
Placebo  Male  Caucasian  9.888304858  74  81  5  1.666  5.014736175
Placebo  Male  Caucasian  9.258536833  118  81  4  1.323  2.085103989
Placebo  Male  Caucasian  10.53974577  114  84.5  5  1.93  2.303398132
Active  Male  Other  6.50722277  86  80  4  0.805  5.197927475
Active  Male  Caucasian  11.9086728  68  75  5  2.201  1.733133316
Active  Male  Other  6.408668236  78  72  4  0.625  2.023418427
Placebo  Male  Other  6.099430574  116  82.5  4  0.841  -0.089118958
Active  Female  Other  9.272224958  79  90  4  3.718  2.019424438
Placebo  Female  Caucasian  12.79304004  114  90  6  0.193  2.61239624
Active  Male  Caucasian  12.79030242  122  85.5  6  0.045  3.270860672
Active  Male  Caucasian  8.423674992  96  67  5  1.463  3.510000229
Placebo  Male  Caucasian  7.134139108  77  76  5  0.733  1.598516464
Placebo  Male  Caucasian  8.749452475  54  68.5  5  0.045  1.840114593
Active  Male  Other  8.037669733  54  80  6  1.456  2.80421257
Active  Female  Other  9.483136225  112  78  4  0.807  1.332126617
Active  Male  Other  11.11202365  61  68  5  0.091  1.266662598
Placebo  Male  Caucasian  10.30180044  70  89  5  2.274  0.735530853
Active  Male  Other  10.19754253  80  85.5  5  0.045  1.592838287
Active  Male  Caucasian  6.099430574  58  85.5  5  0.467  1.976573945
Active  Male  Other  12.14125693  66  80.5  5  1.217  1.004249573
;
RUN;

PROC GENMOD exactonly DATA=SI1;
CLASS Drug Status ;
MODEL sex  =  Drug_Status / DIST=Binomial LINK=Logit ALPHA=0.05 type3;
EXACT Drug_Status;
RUN;
PROC GENMOD exactonly DATA=SI1;
CLASS Drug Status ;
MODEL EthnicityForAnalysis =  Drug_Status / DIST=Binomial LINK=Logit ALPHA=0.05
type3;
EXACT Drug_Status;
RUN;

proc glm data=SI1;
CLASS Drug_Status;
MODEL Age SB5_FSIQ_Standard_Score V1V2_SRS2T_Total_Score
V1_CGI_Social_Interaction_and_Co V1_AVP_level_pg_mL_ V1_AVPR1a_OXTR = Drug_Status /
e3;
LSmeans Drug_Status / stderr;
run;
```

Table S2. Participants' stable concomitant medications during the 4-week AVP treatment trial.

Medication	AVP (N=17)	Placebo (N=13)
SSRI	1 (6%)	2 (15%)
Other antidepressant	0 (0%)	1 (8%)
Antipsychotic	0 (0%)	1 (8%)
Benzodiazepine	0 (0%)	1 (8%)
Stimulant	2 (12%)	2 (15%)
Anti-epileptic	0 (0%)	1 (8%)
NMDAR antagonist	1 (6%)	0 (0%)
Guanfacine	1 (6%)	3 (23%)
Melatonin	0 (0%)	3 (23%)
Atomoxetine	1 (6%)	0 (0%)

Abbreviations: AVP, arginine vasopressin; SSRI, selective serotonin reuptake inhibitor; NMDAR, N-methyl-D-aspartate receptor. Medication classes are reported as counts and percentages. Fisher's Exact Test was used to test for differences in concomitant medications between the AVP and Placebo treatment groups. No significant differences were discerned.

Table S3. Raw data and SAS code testing whether parents could ascertain treatment condition.

	Actual Drug Status	
Drug Status Parent Prediction	Active	Placebo
Active	9	7
Placebo	8	6

```
DATA SI3; INPUT  Drug_Status &$16. Drug_Status_Parent_Prediction &$16.; Lines;
Placebo  Placebo
Active  Placebo
Placebo  Active
Placebo  Active
Active  Placebo
Placebo  Placebo
Active  Placebo
Active  Active
Placebo  Placebo
Active  Placebo
Placebo  Active
Placebo  Placebo
Placebo  Placebo
Active  Active
Active  Active
Active  Active
Placebo  Active
Active  Active
Placebo  Active
Active  Placebo
Active  Placebo
Placebo  Active
Placebo  Placebo
Active  Active
Active  Active
Active  Active
Placebo  Active
Active  Active
Active  Placebo
Active  Placebo
;
RUN;


PROC genmod  DATA=SI3 plots= none;
CLASS Drug_Status_Parent_Prediction;
MODEL  Drug_Status =  Drug_Status_Parent_Prediction/ DIST=Binomial LINK=LOGIT
type3;
lsmeans Drug_Status_Parent_Prediction / ilink;
RUN;
```

Table S4. Raw data and SAS code testing whether bottle weights differed between treatment conditions.

```
DATA SI4; INPUT  Tx &$16. AvgOfBottle_Weight_mg; Lines;
RCTPBO  57517.2
RCTAVP  70784.1
RCTPBO  69670.7
RCTPBO  59973.05
RCTPBO  59014
RCTAVP  60748.25
RCTAVP  64249.3
RCTPBO  60702
RCTAVP  62387.25
RCTPBO  56917.55
RCTPBO  55630.5
RCTAVP  61070.75
RCTPBO  54861.65
RCTAVP  60157.5
RCTAVP  59819.45
RCTPBO  58171.45
RCTPBO  58288.4
RCTAVP  55150
RCTAVP  53250
RCTPBO  59700
RCTAVP  56150.15
RCTAVP  57083.5
RCTAVP  61477.65
;
RUN;

PROC GLM  DATA=SI4;
CLASS Tx;
MODEL  AvgOfBottle_Weight_mg =  Tx/ e3;
LSMEANS Tx / stderr;
RUN;
```

Table S5. Raw data and SAS code for Fig. 2A and associated analyses.

```
DATA SI5; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR
V1V2_SRS2T_Total_Score V1V2_V6_SRS2T_Total_Score; Lines;
Placebo  0  A  68  1.037  0.012833169  3.085927963  80  18
Active  12  B  70  0.598  0.040816327  1.885335923  81.5  -0.5
Placebo  0  B  98  0.514  0.5  4.152868271  88  19
Placebo  0  B  118  2.085  0.040816327  1.085920333  90  15
Active  16  A  58  0.869  0.012833169  4.076757431  71  -2
Placebo  0  B  74  2.209  0.024691358  2.30529213  78.5  -0.5
Active  12  B  88  4.028  0.055555556  0.052930832  81  5
Active  12  B  66  2.922  2  2.47912407  81  7
Placebo  0  B  99  1.811  0.00617284  1.979845047  90  1
Active  16  B  78  1.148  0.125  2.046735764  66.5  0.5
Placebo  0  B  74  1.666  0.08  5.014736175  81  15
Placebo  0  B  118  1.323  0.00295858  2.085103989  81  -9
Placebo  0  B  114  1.93  0.5  2.303398132  84.5  -0.5
Active  12  A  86  0.805  2  5.197927475  80  24
Active  16  B  68  2.201  0.125  1.733133316  75  24
Active  12  A  78  0.625  0.02  2.023418427  72  -1
Placebo  0  A  116  0.841  0.001953125  -0.089118958  82.5  -0.5
Active  12  A  79  3.718  0.024691358  2.019424438  90  14
Placebo  0  B  114  0.193  0.02  2.61239624  90  24
Active  16  B  122  0.045  0.5  3.270860672  85.5  0.5
Active  12  B  96  1.463  0.055555556  3.510000229  67  5
Placebo  0  B  77  0.733  0.02  1.598516464  76  14
Placebo  0  B  54  0.045  0.5  1.840114593  68.5  3.5
Active  12  A  54  1.456  0.010204082  2.80421257  80  1
Active  12  A  112  0.807  0.125  1.332126617  78  14
Active  16  A  61  0.091  0.012833169  1.266662598  68  7
Placebo  0  B  70  2.274  0.012833169  0.735530853  89  0
Active  16  A  80  0.045  0.002081165  1.592838287  85.5  10.5
Active  12  B  58  0.467  0.5  1.976573945  85.5  -1.5
Active  16  A  66  1.217  0.013888889  1.004249573  80.5  6.5
;
RUN;

PROC GLM  DATA=SI5;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V1V2_V6_SRS2T_Total_Score =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1V2_SRS2T_Total_Score/ ss3 ;

/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
```

```
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S6. Raw data and SAS code testing treatment effects for the SRS-2 using an unweighted analysis.

```
DATA SI6; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR
V1V2_SRS2T_Total_Score V1V2_V6_SRS2T_Total_Score; Lines;
Placebo  0  A  68  1.037  0.012833169  3.085927963  80  18
Active  12  B  70  0.598  0.040816327  1.885335923  81.5  -0.5
Placebo  0  B  98  0.514  0.5  4.152868271  88  19
Placebo  0  B  118  2.085  0.040816327  1.085920333  90  15
Active  16  A  58  0.869  0.012833169  4.076757431  71  -2
Placebo  0  B  74  2.209  0.024691358  2.30529213  78.5  -0.5
Active  12  B  88  4.028  0.055555556  0.052930832  81  5
Active  12  B  66  2.922  2  2.47912407  81  7
Placebo  0  B  99  1.811  0.00617284  1.979845047  90  1
Active  16  B  78  1.148  0.125  2.046735764  66.5  0.5
Placebo  0  B  74  1.666  0.08  5.014736175  81  15
Placebo  0  B  118  1.323  0.00295858  2.085103989  81  -9
Placebo  0  B  114  1.93  0.5  2.303398132  84.5  -0.5
Active  12  A  86  0.805  2  5.197927475  80  24
Active  16  B  68  2.201  0.125  1.733133316  75  24
Active  12  A  78  0.625  0.02  2.023418427  72  -1
Placebo  0  A  116  0.841  0.001953125  -0.089118958  82.5  -0.5
Active  12  A  79  3.718  0.024691358  2.019424438  90  14
Placebo  0  B  114  0.193  0.02  2.61239624  90  24
Active  16  B  122  0.045  0.5  3.270860672  85.5  0.5
Active  12  B  96  1.463  0.055555556  3.510000229  67  5
Placebo  0  B  77  0.733  0.02  1.598516464  76  14
Placebo  0  B  54  0.045  0.5  1.840114593  68.5  3.5
Active  12  A  54  1.456  0.010204082  2.80421257  80  1
Active  12  A  112  0.807  0.125  1.332126617  78  14
Active  16  A  61  0.091  0.012833169  1.266662598  68  7
Placebo  0  B  70  2.274  0.012833169  0.735530853  89  0
Active  16  A  80  0.045  0.002081165  1.592838287  85.5  10.5
Active  12  B  58  0.467  0.5  1.976573945  85.5  -1.5
Active  16  A  66  1.217  0.013888889  1.004249573  80.5  6.5
;
RUN;

PROC GLM  DATA=SI6;

CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) at the intercept, not at the mean or weighted mean values of
interacting terms. Thus these marginal terms should be disregarded in the SAS ANOVA
table output. */

MODEL  V1V2_V6_SRS2T_Total_Score =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1V2_SRS2T_Total_Score/ ss3 ;
RUN;
```

Table S7. Raw data and SAS code testing treatment effects for the SCI subscale of the SRS-2.

```
DATA SI7; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR
V1V2_SRS2T_SCI V1V2_V6_SRS2T_SCI; Lines;
Placebo  0  Other  68  1.037  0.012833169  3.085927963  79  16
Active  12  Caucasian  70  0.598  0.040816327  1.885335923  80.5  -0.5
Placebo  0  Caucasian  98  0.514  0.5  4.152868271  86  20
Placebo  0  Caucasian  118  2.085  0.040816327  1.085920333  88  15
Active  16  Other  58  0.869  0.012833169  4.076757431  71  0
Placebo  0  Caucasian  74  2.209  0.024691358  2.30529213  75  0
Active  12  Caucasian  88  4.028  0.055555556  0.052930832  80.5  4.5
Active  12  Caucasian  66  2.922  2  2.47912407  80.5  8.5
Placebo  0  Caucasian  99  1.811  0.00617284  1.979845047  89  2
Active  16  Caucasian  78  1.148  0.125  2.046735764  69  2
Placebo  0  Caucasian  74  1.666  0.08  5.014736175  76.5  11.5
Placebo  0  Caucasian  118  1.323  0.00295858  2.085103989  79.5  -10.5
Placebo  0  Caucasian  114  1.93  0.5  2.303398132  85  -1
Active  12  Other  86  0.805  2  5.197927475  77.5  22.5
Active  16  Caucasian  68  2.201  0.125  1.733133316  75  25
Active  12  Other  78  0.625  0.02  2.023418427  69.5  0.5
Placebo  0  Other  116  0.841  0.001953125  -0.089118958  84.5  -1.5
Active  12  Other  79  3.718  0.024691358  2.019424438  89.5  14.5
Placebo  0  Caucasian  114  0.193  0.02  2.61239624  90  23
Active  16  Caucasian  122  0.045  0.5  3.270860672  85.5  0.5
Active  12  Caucasian  96  1.463  0.055555556  3.510000229  64.5  3.5
Placebo  0  Caucasian  77  0.733  0.02  1.598516464  75  15
Placebo  0  Caucasian  54  0.045  0.5  1.840114593  70  4
Active  12  Other  54  1.456  0.010204082  2.80421257  80.5  0.5
Active  12  Other  112  0.807  0.125  1.332126617  79  13
Active  16  Other  61  0.091  0.012833169  1.266662598  69  7
Placebo  0  Caucasian  70  2.274  0.012833169  0.735530853  87  0
Active  16  Other  80  0.045  0.002081165  1.592838287  85  10
Active  12  Caucasian  58  0.467  0.5  1.976573945  84.5  -1.5
Active  16  Other  66  1.217  0.013888889  1.004249573  78  6
;
RUN;

PROC GLM  DATA=SI7;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V1V2_V6_SRS2T_SCI =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1V2_SRS2T_SCI/ ss3 ;

/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
```

```
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S8. Raw data and SAS code correlating parent SRS-2 ratings with clinician CGI evaluations.

```
DATA SI8; INPUT  V6_CGI_Social_Interaction_and_Co V1V2_V6_SRS2T_SCI; Lines;
3  -0.5
4  0
4  4.5
3  8.5
4  2
1  22.5
2  25
4  0.5
2  14.5
4  0.5
4  3.5
4  0.5
3  13
3  7
3  10
4  -1.5
4  6
;
RUN;


proc corr Data=SI8;
VAR V1V2_V6_SRS2T_SCI;
with V6_CGI_Social_Interaction_and_Co;

run;
```

Table S9. Raw data and SAS code for Fig. 2B and associated analyses.

```
DATA SI9; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR
V6_CGI_Social_Interaction_and_C2; Lines;
Placebo  0  Other  68  1.037  0.012833169  3.085927963  4
Active  12  Caucasian  70  0.598  0.040816327  1.885335923  3
Placebo  0  Caucasian  98  0.514  0.5  4.152868271  3
Placebo  0  Caucasian  118  2.085  0.040816327  1.085920333  3
Active  16  Other  58  0.869  0.012833169  4.076757431  4
Placebo  0  Caucasian  74  2.209  0.024691358  2.30529213  4
Active  12  Caucasian  88  4.028  0.055555556  0.052930832  4
Active  12  Caucasian  66  2.922  2  2.47912407  3
Placebo  0  Caucasian  99  1.811  0.00617284  1.979845047  4
Active  16  Caucasian  78  1.148  0.125  2.046735764  4
Placebo  0  Caucasian  74  1.666  0.08  5.014736175  3
Placebo  0  Caucasian  118  1.323  0.00295858  2.085103989  4
Placebo  0  Caucasian  114  1.93  0.5  2.303398132  4
Active  12  Other  86  0.805  2  5.197927475  1
Active  16  Caucasian  68  2.201  0.125  1.733133316  2
Active  12  Other  78  0.625  0.02  2.023418427  4
Placebo  0  Other  116  0.841  0.001953125  -0.089118958  2
Active  12  Other  79  3.718  0.024691358  2.019424438  2
Placebo  0  Caucasian  114  0.193  0.02  2.61239624  2
Active  16  Caucasian  122  0.045  0.5  3.270860672  4
Active  12  Caucasian  96  1.463  0.055555556  3.510000229  4
Placebo  0  Caucasian  77  0.733  0.02  1.598516464  3
Placebo  0  Caucasian  54  0.045  0.5  1.840114593  4
Active  12  Other  54  1.456  0.010204082  2.80421257  4
Active  12  Other  112  0.807  0.125  1.332126617  3
Active  16  Other  61  0.091  0.012833169  1.266662598  3
Placebo  0  Caucasian  70  2.274  0.012833169  0.735530853  3
Active  16  Other  80  0.045  0.002081165  1.592838287  3
Active  12  Caucasian  58  0.467  0.5  1.976573945  4
Active  16  Other  66  1.217  0.013888889  1.004249573  4
;
RUN;

PROC GLM  DATA=SI9;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V6_CGI_Social_Interaction_and_C2 =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR / ss3 ;

/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
```

```
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S10. Raw data and SAS code for Fig. 2C and associated analyses.

```
DATA SI10; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL V1_AVPR1a_OXTR V1_RMET_Total
V1_V6_RMET_Total; Lines;
Placebo  0  Other  68  1.037  3.085927963  14  4
Active  12  Caucasian  70  0.598  1.885335923  .  .
Placebo  0  Caucasian  98  0.514  4.152868271  18  -2
Placebo  0  Caucasian  118  2.085  1.085920333  9  0
Active  16  Other  58  0.869  4.076757431  4  -1
Placebo  0  Caucasian  74  2.209  2.30529213  17  -3
Active  12  Caucasian  88  4.028  0.052930832  .  .
Active  12  Caucasian  66  2.922  2.47912407  .  .
Placebo  0  Caucasian  99  1.811  1.979845047  22  3
Active  16  Caucasian  78  1.148  2.046735764  17  1
Placebo  0  Caucasian  74  1.666  5.014736175  .  .
Placebo  0  Caucasian  118  1.323  2.085103989  13  4
Placebo  0  Caucasian  114  1.93  2.303398132  19  .
Active  12  Other  86  0.805  5.197927475  .  .
Active  16  Caucasian  68  2.201  1.733133316  4  -6
Active  12  Other  78  0.625  2.023418427  .  .
Placebo  0  Other  116  0.841  -0.089118958  9  1
Active  12  Other  79  3.718  2.019424438  8  0
Placebo  0  Caucasian  114  0.193  2.61239624  20  -4
Active  16  Caucasian  122  0.045  3.270860672  17  -2
Active  12  Caucasian  96  1.463  3.510000229  9  .
Placebo  0  Caucasian  77  0.733  1.598516464  .  .
Placebo  0  Caucasian  54  0.045  1.840114593  .  .
Active  12  Other  54  1.456  2.80421257  .  .
Active  12  Other  112  0.807  1.332126617  17  -6
Active  16  Other  61  0.091  1.266662598  7  -1
Placebo  0  Caucasian  70  2.274  0.735530853  18  4
Active  16  Other  80  0.045  1.592838287  .  .
Active  12  Caucasian  58  0.467  1.976573945  .  .
Active  16  Other  66  1.217  1.004249573  .  .
;
RUN;

PROC GLM  DATA=SI10;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) at the intercept, not at the mean or weighted mean values of
interacting terms. Thus these marginal terms should be disregarded in the SAS ANOVA
table output. */

MODEL  V1V2_V6_SRS2T_Total_Score =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1V2_SRS2T_Total_Score/ ss3 ;
RUN;
```

```
/* Here we figure the LSMs for the drug treatment at the correct mean of Baseline
AVP */

lsmeans Drug_Status/  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct mean of Baseline AVP. Note the same p-value to the TDIFF command above, and
that the F value is the square of the T value generate by the TDIFF command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;


RUN;
```

Table S11. Raw data and SAS code for Fig. 2D and associated analyses.

```
DATA SI11; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL V1_Total_Correct_Facial_Emotion
V1_V6_Total_Correct_Facial_Emot V1_AVPR1a_OXTR; Lines;
Placebo  0  Other  68  1.037  26  9  3.085927963
Active  12  Caucasian  70  0.598  .  .  1.885335923
Placebo  0  Caucasian  98  0.514  36  -3  4.152868271
Placebo  0  Caucasian  118  2.085  32  20  1.085920333
Active  16  Other  58  0.869  6  -3  4.076757431
Placebo  0  Caucasian  74  2.209  30  -1  2.30529213
Active  12  Caucasian  88  4.028  .  .  0.052930832
Active  12  Caucasian  66  2.922  5  .  2.47912407
Placebo  0  Caucasian  99  1.811  37  -1  1.979845047
Active  16  Caucasian  78  1.148  34  -6  2.046735764
Placebo  0  Caucasian  74  1.666  .  .  5.014736175
Placebo  0  Caucasian  118  1.323  35  5  2.085103989
Placebo  0  Caucasian  114  1.93  23  .  2.303398132
Active  12  Other  86  0.805  .  .  5.197927475
Active  16  Caucasian  68  2.201  19  2  1.733133316
Active  12  Other  78  0.625  .  .  2.023418427
Placebo  0  Other  116  0.841  24  16  -0.089118958
Active  12  Other  79  3.718  3  -9  2.019424438
Placebo  0  Caucasian  114  0.193  34  -4  2.61239624
Active  16  Caucasian  122  0.045  28  -9  3.270860672
Active  12  Caucasian  96  1.463  24  .  3.510000229
Placebo  0  Caucasian  77  0.733  5  0  1.598516464
Placebo  0  Caucasian  54  0.045  .  .  1.840114593
Active  12  Other  54  1.456  .  .  2.80421257
Active  12  Other  112  0.807  38  1  1.332126617
Active  16  Other  61  0.091  6  1  1.266662598
Placebo  0  Caucasian  70  2.274  39  2  0.735530853
Active  16  Other  80  0.045  .  .  1.592838287
Active  12  Caucasian  58  0.467  .  .  1.976573945
Active  16  Other  66  1.217  .  .  1.004249573
;
RUN;


PROC GLM  DATA=SI11;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) at the intercept, not at the mean or weighted mean values of
interacting terms. Thus these marginal terms should be disregarded in the SAS ANOVA
table output. */

MODEL  V1_V6_Total_Correct_Facial_Emot =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1_Total_Correct_Facial_Emotion / ss3 ;
```

```
/* Here we figure the LSMs for the drug treatment at the correct mean of Baseline
AVP */

lsmeans Drug_Status/  tdiff stderr e;

/* This contrast tests for the difference between the drug treatments at the
correct mean of Baseline AVP. Note the same p-value to the TDIFF command above, and
that the F value is the square of the T value generate by the TDIFF command */

contrast "Test drug treatment effect at mean baseline AVP = 1.28817647"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.64408824 0.64408824 -
1.28817647
      Drug_Status*V1_AVP_level_pg_mL 1.28817647 -1.28817647;
RUN;
```

Table S12. Raw data and SAS code for Fig. 2E and associated analyses.

```
DATA SI12; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL V1_Spence_Anxiety_Total_Raw_Scor
V1_V6_Spence_Anxiety_Total_Raw_S WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR; Lines;
Placebo  0  Other  68  1.037  4  -1  0.012833169  3.085927963
Active  12  Caucasian  70  0.598  16  2  0.040816327  1.885335923
Placebo  0  Caucasian  98  0.514  31  22  0.5  4.152868271
Placebo  0  Caucasian  118  2.085  18  7  0.040816327  1.085920333
Active  16  Other  58  0.869  25  1  0.012833169  4.076757431
Placebo  0  Caucasian  74  2.209  10  2  0.024691358  2.30529213
Active  12  Caucasian  88  4.028  24  0  0.055555556  0.052930832
Active  12  Caucasian  66  2.922  16  6  2  2.47912407
Placebo  0  Caucasian  99  1.811  69  20  0.00617284  1.979845047
Active  16  Caucasian  78  1.148  19  2  0.125  2.046735764
Placebo  0  Caucasian  74  1.666  26  8  0.08  5.014736175
Placebo  0  Caucasian  118  1.323  32  -14  0.00295858  2.085103989
Placebo  0  Caucasian  114  1.93  24  -10  0.5  2.303398132
Active  12  Other  86  0.805  56  47  2  5.197927475
Active  16  Caucasian  68  2.201  11  4  0.125  1.733133316
Active  12  Other  78  0.625  5  -1  0.02  2.023418427
Placebo  0  Other  116  0.841  18  -6  0.001953125  -0.089118958
Active  12  Other  79  3.718  40  20  0.024691358  2.019424438
Placebo  0  Caucasian  114  0.193  25  9  0.02  2.61239624
Active  16  Caucasian  122  0.045  16  -10  0.5  3.270860672
Active  12  Caucasian  96  1.463  6  -1  0.055555556  3.510000229
Placebo  0  Caucasian  77  0.733  12  8  0.02  1.598516464
Placebo  0  Caucasian  54  0.045  7  -2  0.5  1.840114593
Active  12  Other  54  1.456  28  4  0.010204082  2.80421257
Active  12  Other  112  0.807  31  21  0.125  1.332126617
Active  16  Other  61  0.091  6  1  0.012833169  1.266662598
Placebo  0  Caucasian  70  2.274  9  0  0.012833169  0.735530853
Active  16  Other  80  0.045  22  11  0.002081165  1.592838287
Active  12  Caucasian  58  0.467  25  11  0.5  1.976573945
Active  16  Other  66  1.217  9  -1  0.013888889  1.004249573
;
RUN;

PROC GLM  DATA=SI12;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V1_V6_Spence_Anxiety_Total_Raw_S =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1_Spence_Anxiety_Total_Raw_Scor/ ss3 ;
```

```
/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S13. Raw data and SAS code for Fig. 2F and associated analyses.

```
DATA SI13; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL V1_RBSR_Overall_Score
V1_V6_RBSR_Overall_Score WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR; Lines;
Placebo  0  Other  68  1.037  5  -5  0.012833169  3.085927963
Active  12  Caucasian  70  0.598  43  13  0.040816327  1.885335923
Placebo  0  Caucasian  98  0.514  30  18  0.5  4.152868271
Placebo  0  Caucasian  118  2.085  .  .  0.040816327  1.085920333
Active  16  Other  58  0.869  10  -8  0.012833169  4.076757431
Placebo  0  Caucasian  74  2.209  20  -1  0.024691358  2.30529213
Active  12  Caucasian  88  4.028  35  26  0.055555556  0.052930832
Active  12  Caucasian  66  2.922  29  9  2  2.47912407
Placebo  0  Caucasian  99  1.811  95  1  0.00617284  1.979845047
Active  16  Caucasian  78  1.148  9  3  0.125  2.046735764
Placebo  0  Caucasian  74  1.666  45  17  0.08  5.014736175
Placebo  0  Caucasian  118  1.323  29  -14  0.00295858  2.085103989
Placebo  0  Caucasian  114  1.93  19  10  0.5  2.303398132
Active  12  Other  86  0.805  41  32  2  5.197927475
Active  16  Caucasian  68  2.201  21  10  0.125  1.733133316
Active  12  Other  78  0.625  18  -2  0.02  2.023418427
Placebo  0  Other  116  0.841  19  15  0.001953125  -0.089118958
Active  12  Other  79  3.718  30  25  0.024691358  2.019424438
Placebo  0  Caucasian  114  0.193  50  23  0.02  2.61239624
Active  16  Caucasian  122  0.045  27  -7  0.5  3.270860672
Active  12  Caucasian  96  1.463  13  5  0.055555556  3.510000229
Placebo  0  Caucasian  77  0.733  26  16  0.02  1.598516464
Placebo  0  Caucasian  54  0.045  14  6  0.5  1.840114593
Active  12  Other  54  1.456  28  7  0.010204082  2.80421257
Active  12  Other  112  0.807  11  11  0.125  1.332126617
Active  16  Other  61  0.091  6  0  0.012833169  1.266662598
Placebo  0  Caucasian  70  2.274  19  1  0.012833169  0.735530853
Active  16  Other  80  0.045  35  -1  0.002081165  1.592838287
Active  12  Caucasian  58  0.467  41  -10  0.5  1.976573945
Active  16  Other  66  1.217  46  16  0.013888889  1.004249573
;
RUN;

PROC GLM  DATA=SI13;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V1_V6_RBSR_Overall_Score =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1_RBSR_Overall_Score/ ss3 ;
```

```
/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S14. Raw data and SAS code testing treatment effects for the RRB subscale of the SRS-2.

```
DATA SI14; INPUT  Drug_Status &$16. Dose_IU_BID EthnicityForAnalysis &$16.
SB5_FSIQ_Standard_Score V1_AVP_level_pg_mL WLS_inv_var_of_v1v2_SRST V1_AVPR1a_OXTR
V1V2_SRS2T_RRB V1V2_V6_SRS2T_RRB; Lines;
Placebo  0  Other  68  1.037  0.012833169  3.085927963  78  17
Active  12  Caucasian  70  0.598  0.040816327  1.885335923  80  2
Placebo  0  Caucasian  98  0.514  0.5  4.152868271  90  8
Placebo  0  Caucasian  118  2.085  0.040816327  1.085920333  90  10
Active  16  Other  58  0.869  0.012833169  4.076757431  69  -6
Placebo  0  Caucasian  74  2.209  0.024691358  2.30529213  87  -2
Active  12  Caucasian  88  4.028  0.055555556  0.052930832  78  6
Active  12  Caucasian  66  2.922  2  2.47912407  79  4
Placebo  0  Caucasian  99  1.811  0.00617284  1.979845047  90  0
Active  16  Caucasian  78  1.148  0.125  2.046735764  56  -3
Placebo  0  Caucasian  74  1.666  0.08  5.014736175  90  22
Placebo  0  Caucasian  118  1.323  0.00295858  2.085103989  81  -9
Placebo  0  Caucasian  114  1.93  0.5  2.303398132  78  0
Active  12  Other  86  0.805  2  5.197927475  84.5  25.5
Active  16  Caucasian  68  2.201  0.125  1.733133316  72  19
Active  12  Other  78  0.625  0.02  2.023418427  80.5  -2.5
Placebo  0  Other  116  0.841  0.001953125  -0.089118958  68  0
Active  12  Other  79  3.718  0.024691358  2.019424438  90  16
Placebo  0  Caucasian  114  0.193  0.02  2.61239624  86  24
Active  16  Caucasian  122  0.045  0.5  3.270860672  82.5  0.5
Active  12  Caucasian  96  1.463  0.055555556  3.510000229  73.5  7.5
Placebo  0  Caucasian  77  0.733  0.02  1.598516464  78  10
Placebo  0  Caucasian  54  0.045  0.5  1.840114593  62.5  3.5
Active  12  Other  54  1.456  0.010204082  2.80421257  75  2
Active  12  Other  112  0.807  0.125  1.332126617  70  12
Active  16  Other  61  0.091  0.012833169  1.266662598  66  9
Placebo  0  Caucasian  70  2.274  0.012833169  0.735530853  90  0
Active  16  Other  80  0.045  0.002081165  1.592838287  86  13
Active  12  Caucasian  58  0.467  0.5  1.976573945  83.5  -3.5
Active  16  Other  66  1.217  0.013888889  1.004249573  83.5  7.5
;
RUN;

PROC GLM  DATA=SI14;
WEIGHT WLS_inv_var_of_v1v2_SRST;
CLASS Drug_Status Dose_IU_BID EthnicityForAnalysis;

/* Note that SAS calculates F tests of marginal terms (e.g. main effects contained
in an interaction) incorrectly for weighted least squares, and these marginal terms
should be disregarded in the SAS ANOVA table output. Appropriate tests, equivalent
to those performed by JMP are explicitly specified in the LSMEANS and CONTRAST
statements below. */

MODEL  V1V2_V6_SRS2T_RRB =  Dose_IU_BID(Drug_Status )
      Drug_Status
      EthnicityForAnalysis
      SB5_FSIQ_Standard_Score
      V1_AVP_level_pg_mL
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status )
      Drug_Status*V1_AVP_level_pg_mL
      V1_AVPR1a_OXTR
      V1V2_SRS2T_RRB / ss3 ;
```

```
/* Note that SAS defaults to incorrectly using the simple mean of X variables in
post-hoc tests, rather than the weighted mean of X variables that should follow
from the WEIGHT statement. JMP performs post-hoc test correctly. To produce the
correct post-hoc tests and thus tests of marginal terms, the correct weighted mean
must be explicitly specified. */

/* Here we figure the LSMs for the drug treatment at the correct weighted mean of
Baseline AVP */

lsmeans Drug_Status/ at V1_AVP_level_pg_mL=1.40253  tdiff stderr;

/* This contrast tests for the difference between the drug treatments at the
correct weighted mean of Baseline AVP. Note the same p-value to the TDIFF command
above, and that the F value is the square of the T value generate by the TDIFF
command */

contrast "Test drug treatment effect at mean baseline AVP = 1.40253"
Dose_IU_BID(Drug_Status ) 0.5 0.5 -1
      Drug_status 1 -1
      Dose_IU_BID*V1_AVP_level_pg_mL(Drug_Status ) 0.701265 0.701265 -1.40253
      Drug_Status*V1_AVP_level_pg_mL 1.40253 -1.40253;

/* This CONTRAST statement tests the slope of the BaselineAVP*Drug for the Active
drug */

contrast "Does baseline AVP predict treatment response in AVP treated Sx"
V1_AVP_level_pg_mL 1 Drug_Status*V1_AVP_level_pg_mL 1 0;
RUN;
```

Table S15. Change from baseline in the safety assessments for the 4-week AVP treatment trial.

Measure	Drug Treatment main effect	Change from baseline LSM +/- SE	
		AVP	Placebo
Vital Sign			
BP, Systolic, Sitting (mmHg)	$F_{1,28}$=2.9584; P=0.0966	5.5 ± 2.53	-1.1 ± 2.89
BP, Diastolic, Sitting (mmHg)	$F_{1,28}$=2.5600; P=0.1200	3.2 ± 2.09	-1.8 ± 2.39
BP, Systolic, Standing (mmHg)	$F_{1,28}$=0.3844; P=0.5397	1.9 ± 2.38	-0.3 ± 2.73
BP, Diastolic, Standing (mmHg)	$F_{1,28}$=0.0289; P=0.8700	0.1 ± 2.31	-0.5 ± 2.64
BP Change Systolic (Standing-Sitting)	$F_{1,28}$=1.0816; P=0.3069	-3.6 ± 2.76	0.8 ± 3.15
BP Change Diastolic (Standing-Sitting)	$F_{1,28}$=1.2544; P=0.2726	-3.1 ± 2.65	1.4 ± 3.03
Pulse sitting (beats per minute)	$F_{1,28}$=0.8836; P=0.3563	1.9 ± 3.87	7.5 ± 4.43
Pulse standing (beats per minute)	$F_{1,28}$=0.9604; P=0.3359	4.0 ± 3.57	9.3 ± 4.08
Pulse change (beats per minute)	$F_{1,28}$=0.0025; P=0.9598	2.1 ± 2.75	1.8 ± 3.15
Temperature (°F)	$F_{1,28}$=2.3409; P=0.1369	0.2 ± 0.17	-0.2 ± 0.19
Electrocardiogram			
Heart Rate (bpm)	$F_{1,26}$=0.4096; P=0.5272	-2.5 ± 3.75	1.2 ± 4.32
P Duration (ms)	$F_{1,25}$=0.2025; P=0.6600	-2.6 ± 5.76	1.5 ± 6.95
PR Interval (ms)	$F_{1,26}$=0.3481; P=0.5586	-4.6 ± 6.40	1.2 ± 7.39
QRS Interval (ms)	$F_{1,26}$=0.3844; P=0.5421	0.4 ± 1.55	1.8 ± 1.78
QT Interval (ms)	$F_{1,26}$=0.9604; P=0.3378	3.5 ± 5.53	-4.8 ± 6.39
Bazett's Corrected QT Interval (ms)	$F_{1,26}$<0.0001; P=0.9979	-1.9 ± 5.07	-1.9 ± 5.86
Clinical Chemistry			
Sodium (mmol/L)	$F_{1,28}$=0.0081; P=0.9328	0.24 ± 0.63	0.15 ± 0.72
Potassium (mmol/L)	$F_{1,28}$=0.2601; P=0.6132	0.15 ± 0.11	0.06 ± 0.13
Chloride (mmol/L)	$F_{1,28}$=2.3716; P=0.1348	1.0 ± 0.56	-0.31 ± 0.64
CO_2 (mmol/L)	$F_{1,28}$=1.4400; P=0.2395	-0.12 ± 0.57	0.92 ± 0.65
Anion Gap (mmol/L)	$F_{1,28}$=0.0256; P=0.8762	-0.65 ± 0.78	-0.46 ± 0.89
Glucose (mg/dL)	$F_{1,28}$=0.2704; P=0.6099	2.2 ± 4.41	5.7 ± 5.04
Creatinine (mg/dL)	$F_{1,28}$=1.2321; P=0.2756	-0.017 ± 0.03	0.027 ± 0.03
Urea Nitrogen (mg/dL)	$F_{1,28}$=2.4025; P=0.1314	-1.3 ± 0.78	0.54 ± 0.89
Calcium (mg/dL)	$F_{1,28}$=2.3716; P=0.1355	0.047 ± 0.07	0.20 ± 0.07
Osmolality (Serum) (mOsm/kg)	$F_{1,28}$=2.6244; P=0.1158	0.18 ± 1.01	-2.3 ± 1.15
Osmolality (Urine) (mOsm/kg)	$F_{1,25}$=0.0625; P=0.8027	8.5 ± 82.6	-23 ± 92.3
Physiological			
Height (centimeters)	$F_{1,28}$=2.0736; P=0.1619	0.8 ± 0.23	0.3 ± 0.27
Weight (kilograms)	$F_{1,28}$=0.0225; P=0.8809	0.3 ± 0.30	0.2 ± 0.34

Abbreviations: LSM, Least Squares Mean; AVP, arginine vasopressin; BP, blood pressure. Within-subject changes from baseline were calculated for each measure, and the effect of treatment tested using a general linear model. No significant effects were discerned.

Table S16. Raw data and SAS code for the data and analyses shown in table S15.

```
DATA Safety_vitals; INPUT  Drug_Status &$ V6_V1_BP_Sys_Sit V6_V1_BP_Dias_Sit
V6_V1_Pulse_bmp_Sit V6_V1_BP_Sys_Stand V6_V1_BP_Dias_Stand V6_V1_Pulse_bmp_Stand
V6_V1_BP_Sys_Delta V6_V1_BP_Dias_Delta V6_V1_Pulse_bmp_Delta V6_V1_Temperature_F
V6_V1_Height_cm V6_V1_Weight_kg; Lines;
Active  -3  -16  3  -7  -14  1  -4  2  -2  -1.3  0.5  0.79
Active  12  10  8  6  1  -6  -6  -9  -14  0.2  0  0.91
Active  8  4  2  -3  -2  26  -11  -6  24  0.8  0.25  0
Active  19  18  6  21  20  -1  2  2  -7  -0.1  0.25  0
Active  8  4  2  3  8  11  -5  4  9  -0.3  2.5  -0.23
Active  -12  -5  -18  -2  0  5  10  5  23  0  1.25  0.68
Active  20  11  -10  6  2  10  -14  -9  20  -0.4  2.5  0.45
Active  -3  8  8  -2  0  9  1  -8  1  0.8  0  -0.23
Active  11  -1  -9  16  2  10  5  3  19  0.7  1.5  0.9
Active  -5  7  -5  9  14  -16  14  7  -11  0.2  1  2.05
Active  5  5  8  11  -9  7  6  -14  -1  -0.2  1.22  -0.85
Active  -5  12  6  3  -19  -7  8  -31  -13  -0.1  -1.5  -4
Active  -13  -9  -16  -9  -5  -14  4  4  2  -0.2  0.2  0.15
Active  15  -8  -13  -14  15  -23  -29  23  -10  0.4  1.5  -0.3
Active  2  -6  30  5  -2  18  3  4  -12  0.5  0.7  0.35
Active  27  17  13  0  -5  14  -27  -22  1  1  1.2  1
Active  8  4  18  -10  -4  24  -18  -8  6  1.2  0.6  3.15
Placebo  3  6  17  1  4  8  -2  -2  -9  1.8  1  -0.23
Placebo  4  5  24  -3  7  14  -7  2  -10  0.5  -0.5  -1.81
Placebo  4  -1  -35  -4  0  -25  -8  1  10  -1  1  0
Placebo  -7  -5  36  -11  3  45  -4  8  9  -0.3  0.25  0
Placebo  -3  -4  -21  -3  2  0  0  6  21  0.3  0  1.13
Placebo  -7  -8  0  7  -7  4  14  1  4  -1.2  1.25  0.23
Placebo  -15  -18  22  -11  1  20  4  19  -2  -0.5  0  -0.45
Placebo  -6  0  26  -5  -1  23  1  -1  -3  0.1  1.5  1.82
Placebo  -8  -2  0  -9  -6  0  -1  -4  0  -0.2  2  0
Placebo  19  5  3  1  -6  8  -18  -11  5  -0.1  -1  0.95
Placebo  0  -4  7  6  1  12  6  5  5  -1.1  -0.9  0.7
Placebo  10  9  16  29  17  8  19  8  -8  -0.7  -0.3  0.3
Placebo  -8  -7  2  -2  -21  4  6  -14  2  -0.3  -0.5  0.15
;
RUN;

PROC GLM  DATA=Safety_vitals ALPHA=0.05 PLOTS=NONE;
CLASS Drug_Status;
MODEL  V6_V1_BP_Sys_Sit V6_V1_BP_Dias_Sit V6_V1_Pulse_bmp_Sit V6_V1_BP_Sys_Stand
V6_V1_BP_Dias_Stand V6_V1_Pulse_bmp_Stand V6_V1_BP_Sys_Delta V6_V1_BP_Dias_Delta
V6_V1_Pulse_bmp_Delta V6_V1_Temperature_F V6_V1_Height_cm V6_V1_Weight_kg
=  Drug_Status / SS3;
lsmeans DRUG_STATUS / STDERR;
RUN;

DATA Safety_clinical_labs; INPUT  Drug_Status &$ V6_V1_Sodium_mmol_L
V6_V1_Potassium_mmol_L V6_V1_Chloride_mmol_L V6_V1_CO2_mmol_L
V6_V1_Anion_Gap_mmol_L V6_V1_Glucose_mg_dL V6_V1_Creatinine_mg_dL
V6_V1_Urea_Nitrogen_mg_dL V6_V1_Calcium_mg_dL V6_V1_Osmolality_Serum_mOsm_kg
V6_V1_Osmolality_Urine_mOsm_kg; Lines;
Active  2  -0.1  2  -1  1  21  0  -1  0.1  -3  7
Active  -1  0.4  3  1  -5  12  0  -7  -0.3  -3  -63
Active  -1  1.1  3  2  -6  -59  -0.1  4  0.1  1  .
Active  3  0.4  3  -1  1  -7  0.1  -2  0.1  5  362
Active  1  -0.2  0  -1  2  -22  0  -6  0.2  -3  -211
Active  -2  0.1  0  2  -4  10  0  -3  -0.1  -4  197
```

```
Active  -7  -0.3  -4  -1  -2  8  0  -1  -0.2  -3  84
Active  0  0.2  0  -1  1  -4  -0.1  -1  0.6  0  422
Active  5  1.2  5  1  -1  27  0  -3  0.3  1  .
Active  0  0  -1  -1  2  -5  -0.1  0  0.3  -1  -259
Active  6  0  4  2  0  10  -0.03  1  0  1  223
Active  1  0.2  2  0  -1  3  0  1  0.1  2  105
Active  0  -0.1  1  1  -2  -5  0.05  4  -0.2  7  319
Active  -1  -0.3  -2  -3  4  8  0.03  -1  0.1  0  -691
Active  1  -0.4  2  -3  2  21  0.06  -3  -0.1  -2  75
Active  -3  0.5  -2  -1  0  17  -0.05  1  0  9  224
Active  0  -0.2  1  2  -3  3  -0.15  -5  -0.2  -4  -667
Placebo  -2  1.1  0  -2  0  13  -0.1  -5  0.8  -5  -175
Placebo  -1  0.5  -3  1  1  15  -0.1  0  -0.1  0  -391
Placebo  0  -0.6  1  2  -3  -5  0.2  -3  0.3  -12  -472
Placebo  2  0  -5  8  -1  38  0.1  5  0.2  -1  112
Placebo  4  0.4  2  -2  4  5  0  0  0.3  1  401
Placebo  2  0  3  5  -6  -11  0.1  1  0  -6  32
Placebo  2  0.2  -2  -2  6  -6  -0.1  -4  0.1  -7  -416
Placebo  1  -0.2  1  0  0  5  0.2  3  0.5  -2  .
Placebo  -2  0.2  1  1  -4  12  -0.1  7  -0.1  3  73
Placebo  -1  0.1  -1  2  -2  -22  0.3  0  0.2  2  49
Placebo  0  -0.4  0  1  -1  17  0.04  0  0.2  -2  -63
Placebo  0  -0.1  -2  -3  5  17  -0.18  1  0.6  -5  178
Placebo  -3  -0.4  1  1  -5  -4  -0.01  2  -0.4  4  398
;
RUN;

PROC GLM  DATA=Safety_clinical_labs ALPHA=0.05 plots=none;
CLASS Drug_Status;
MODEL  V6_V1_Sodium_mmol_L V6_V1_Potassium_mmol_L V6_V1_Chloride_mmol_L
V6_V1_CO2_mmol_L V6_V1_Anion_Gap_mmol_L V6_V1_Glucose_mg_dL V6_V1_Creatinine_mg_dL
V6_V1_Urea_Nitrogen_mg_dL V6_V1_Calcium_mg_dL V6_V1_Osmolality_Serum_mOsm_kg
V6_V1_Osmolality_Urine_mOsm_kg
      =  Drug_Status/ ss3;
lsmeans DRUG_STATUS / STDERR;
RUN;

DATA Safety_ECG; INPUT  Drug_Status &$16. V6_V1_Heart_Rate_bpm_
V6_V1__P_Duration_ms_ V6_V1_PR_Interval_ms_ V6_V1_QRS_Interval_ms_
V6_V1_QT_Interval_ms_ V6_V1_QTCb_Interval_ms_; Lines;
Active  -4  -4  3  -5  11  6
Active  -18  5  17  -1  5  -38
Active  -10  4  -5  15  7  -12
Active  6  -70  -86  -6  5  19
Active  .  .  .  .  .  .
Active  -21  22  5  3  46  3
Active  -8  6  4  4  11  -3
Active  -9  -1  -1  -3  8  -10
Active  0  7  -1  -5  -15  -19
Active  -10  -15  -13  6  2  -26
Active  12  2  1  2  -9  12
Active  4  0  1  5  1  12
Active  -14  1  -7  -14  23  -4
Active  15  12  9  -2  -17  7
Active  11  6  7  5  4  33
Active  -11  2  1  6  17  0
Active  17  -18  -9  -4  -43  -11
Placebo  -12  .  -34  5  -13  -43
Placebo  12  -21  -19  6  -12  23
Placebo  23  -21  -1  6  -35  7
Placebo  30  -13  -9  -4  -50  19
```

```
Placebo  .  .  .  .  .  .
Placebo  -19  8  0  11  7  -41
Placebo  5  -8  -2  8  -12  -1
Placebo  9  -7  -5  -4  -3  14
Placebo  6  -12  -11  -2  13  29
Placebo  5  75  86  -5  -3  9
Placebo  0  4  5  -1  -12  -15
Placebo  -37  11  5  0  52  -14
Placebo  -8  0  -1  2  11  -10
;
RUN;

PROC GLM  DATA=Safety_ECG ALPHA=0.05 plots=none;
CLASS Drug_Status;
MODEL  V6_V1_Heart_Rate_bpm_ V6_V1__P_Duration_ms_ V6_V1_PR_Interval_ms_
V6_V1_QRS_Interval_ms_ V6_V1_QT_Interval_ms_ V6_V1_QTCb_Interval_ms_ =
Drug_Status/ ss3;
lsmeans DRUG_STATUS / STDERR;
RUN;
```