#### **SUPPLEMENTARY FIGURES**

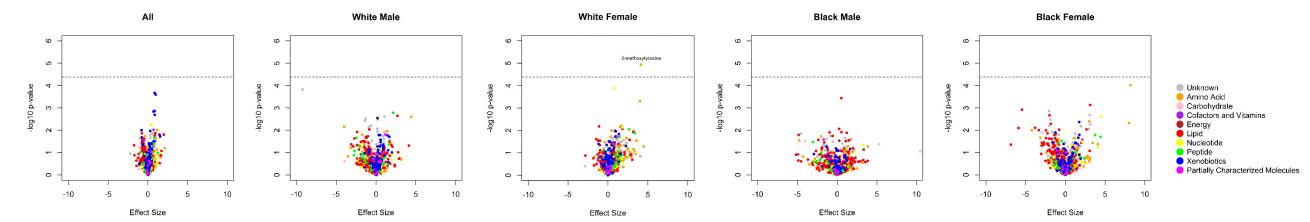
II-Recognition

Supplementary Figure 1. Cognitive domains and the corresponding assessments

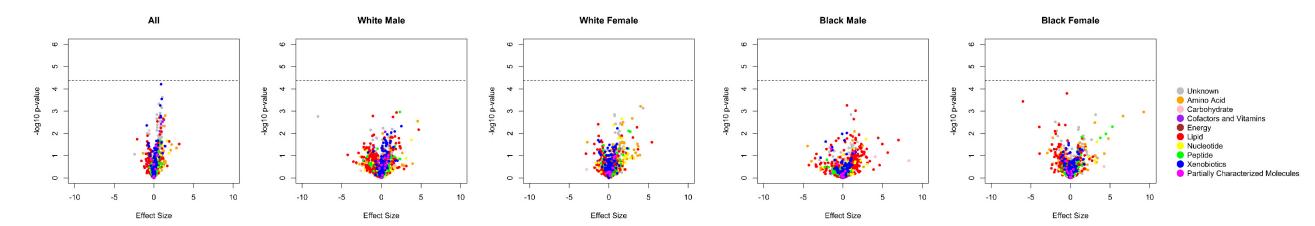
ATTENTION & VERBAL PROCESSING **ABILITY TO** EXECUTIVE CONCENTRATI **FUNCTION MEMORY SPEED** DECODE ON Logical Memory Digit Span Trail Making Digit Coding Word Reading Forward Tests B Logical Memory Digit Span Trail Making Backward Tests A II Logical Memory

### Supplementary Figure 2. Volcano plots of effect sizes versus –log10 P values for all 1202 metabolites among BHS participants, according to cognitive domain

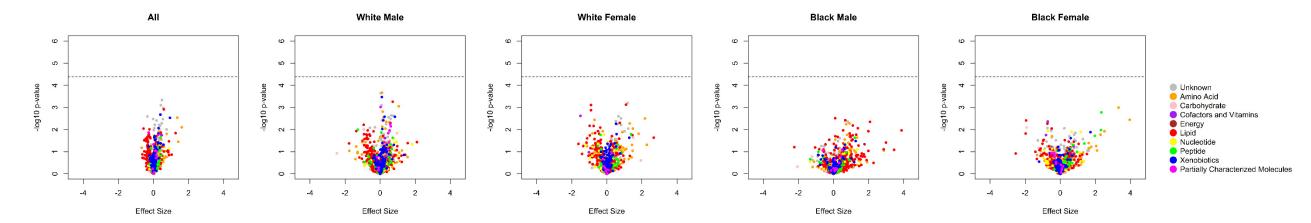
#### 2a) Verbal memory domain (logical memory I test)



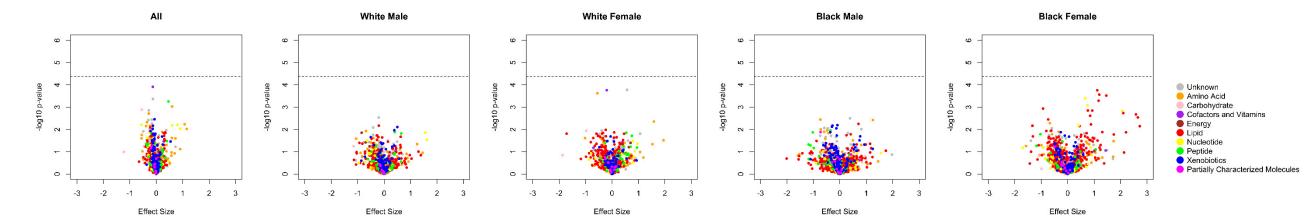
### 2b) Verbal memory domain (logical memory II test)



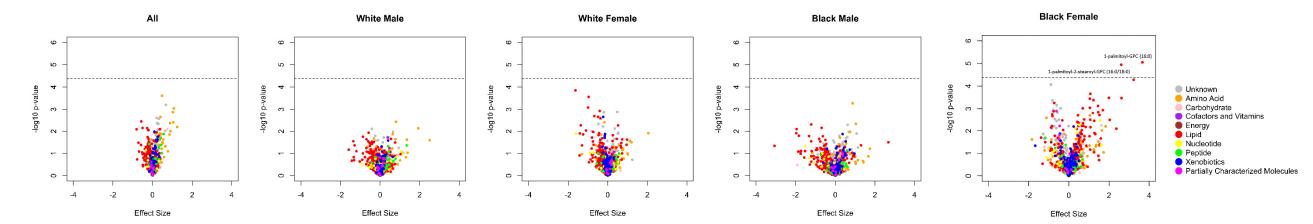
## 2c) Verbal memory domain (logical memory II-recognition)



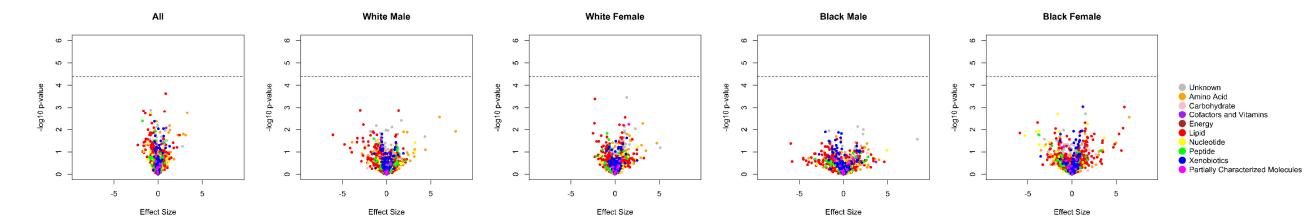
### 2d) Attention and concentration domain (digit span forward test)



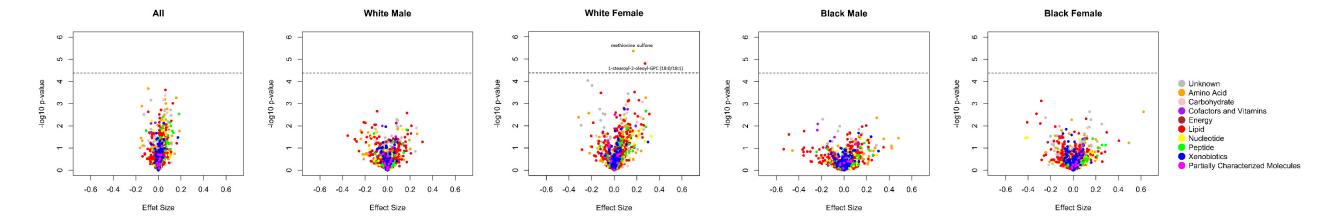
## 2e) Attention and concentration domain (digit span backward)



#### 2f) Ability to decode domain (word reading test)



# 2g) Executive function domain (trail making test B)



#### Supplementary Figure 3. Correlations of metabolite modules with cognition

## 3a) Verbal memory domain (logical memory I test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r (P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r(P)	
Lysophospholipid; Phosphatidylethanolamine (PE); Phosphatidylcholine (PC); Monoacylglycerol; Diacylglycerol	-0.029 (0.3)	-0.11 (0.06)	-0.006 (0.9)	-0.013 (0.9)	0.0034 (1)	1.0
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.028 (0.3)	-0.073 (0.2)	0.015 (0.7)	-0.057 (0.5)	-0.039 (0.5)	
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.023 (0.4)	-0.069 (0.2)	-0.004 (0.9)	0.1 (0.2)	-0.11 (0.08)	- 0.5
Sphingolipid metabolism	-0.0035 (0.9)	-0.008 (0.9)	0.041 (0.4)	0.028 (0.7)	-0.1 (0.1)	
Primary bile acid metabolism; Secondary bile acid metabolism	0.02 (0.5)	0.021 (0.7)	-0.028 (0.5)	0.11 (0.2)	-0.07 <b>4</b> (0.2)	
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	0.015 (0.6)	0.011 (0.9)	0.06 (0.2)	0.032 (0.7)	-0.074 (0.2)	- 0
Food component/Plant	0.0016 (1)	-0.059 (0.3)	-0.012 (0.8)	0.092 (0.3)	0.041 (0.5)	0.5
Androgenic steroids	0.031 (0.3)	-0.0069 (0.9)	0.086 (0.07)	-0.077 (0.4)	0.09 (0.2)	
Androgenic steroids; Pregnenolone steroids; Progestin steroids	-0.012 (0.7)	-0.074 (0.2)	0.00057 (1)	0.031 (0.7)	0.016 (0.8)	-1.0
		Logi	ical Memoi	ry I		

#### 3b) Verbal memory domain (logical memory II test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r (P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r (P)				
Lysophospholipid; Phosphatidylethanolamine (PE); Phosphatidylcholine (PC); Monoacylglycerol; Diacylglycerol	-0.016 (0.6)	-0.098 (0.08)	-0.013 (0.8)	0.12 (0.2)	-0.0082 (0.9)	1.0			
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.023 (0.4)	-0.061 (0.3)	-0.018 (0.7)	0.066 (0.4)	-0.051 (0.4)				
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.008 (0.8)	-0.059 (0.3)	-0.0053 (0.9)	0.17 (0.04)	-0.087 (0.2)	- 0.5			
Sphingolipid metabolism	-0.01 (0.7)	0.00054	0.00 <del>9</del> 7 (0.8)	-0.042 (0.2)	-0.045 (0.5)				
Primary bile acid metabolism; Secondary bile acid metabolism	0.024 (0.4)	0.014 (0.8)	-0.0023 (1)	0.11 (0.2)	-0.092 (0.1)				
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	0.044 (0.1)	0.0096 (0.9)	0.081 (0.09)	0.11 (0.2)	-0.017 (0.8)	-0			
Food component/Plant	0.0073 (0.8)	-0.025 (0.7)	-0.014 (0.8)	0.11 (0.2)	-0.00015 (1)	-0.5			
Androgenic steroids	0.049 (0.09)	0.055 (0.3)	0.062 (0.2)	-0.038 (0.6)	0.11 (0.08)				
Androgenic steroids; Pregnenolone steroids; Progestin steroids	0.027 (0.4)	-0.0051 (0.9)	-0.0035 (0.9)	0.16 (0.05)	0.031 (0.6)	-1.0			
	Logical Memory II								

## 3c) Verbal memory domain (logical memory II-recognition test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r (P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r(P)	
$Ly sophospholipid; Phosphatidylethan olamine (PE); Phosphatidylcholine (PC); \\ Monoacylglycerol; Diacylglycerol$	-0.04 (0.2)	-0.091 (0.1)	-0.074 (0.1)	0.052 (0.5)	0.015 (0.8)	1.0
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.016 (0.6)	-0.018 (0.7)	-0.079 (0.09)	0.0 <b>4</b> 2 (0.6)	0.057 (0.4)	
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.03 (0.3)	-0.066 (0.2)	-0.078 (0.1)	0.11 (0.2)	0.0014 (1)	- 0.5
Sphingolipid metabolism	0.013 (0.7)	0.041 (0.5)	-0.0024 (1)	0.16 (0.05)	-0.067 (0.3)	
Primary bile acid metabolism; Secondary bile acid metabolism	0.0037 (0.9)	-0.054 (0.3)	-0.0042 (0.9)	0.093 (0.3)	-0.035 (0.6)	
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	0.043 (0.1)	0.053 (0.3)	0.02 (0.7)	0. <b>1</b> (0.2)	-0.062 (0.3)	- 0
Food component/Plant	-0.0059 (0.8)	-0.015 (0.8)	-0.043 (0.4)	0.083 (0.3)	-0.016 (0.8)	0.5
Androgenic steroids	0.038 (0.2)	0.06 (0.3)	0.041 (0.4)	-0.045 (0.6)	0.079 (0.2)	
Androgenic steroids; Pregnenolone steroids; Progestin steroids	0.018 (0.5)	0.011 (0.8)	0.0076 (0.9)	0.046 (0.6)	0.011 (0.9)	-1.0
	L	ogical Me	mory II-Re	cognition		

## 3d) Attention and concentration domain (digit span forward test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r (P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r(P)	
Lysophospholipid; Phosphatidylethanolamine (PE); Phosphatidylcholine (PC); Monoacylglycerol; Diacylglycerol	-0.042 (0.2)	-0.053 (0.3)	-0.086 (0.07)	-0.048 (0.6)	0.076 (0.2)	1.0
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.014 (0.6)	-0.013 (0.8)	-0.11 (0.02)	-0.054 (0.5)	0.19 (0.002)	
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.00057 (1)	-0.0068 (0.9)	0.031 (0.5)	0.097 (0.2)	-0.1 (0.1)	- 0.5
Sphingolipid metabolism	-0.00097 (1)	0.014 (0.8)	-0.047 (0.3)	0.056 (0.5)	0.019 (0.8)	
Primary bile acid metabolism; Secondary bile acid metabolism	-0.038 (0.2)	-0.056 (0.3)	0.01 (0.8)	-0.056 (0.5)	-0.099 (0.1)	
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate, Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	-0.062 (0.03)	-0.09 (0.1)	0.0073 (0.9)	-0.098 (0.2)	-0.095 (0.1)	- 0
Food component/Plant	-0.011 (0.7)	-0.0083 (0.9)	0.026 (0.6)	-0.027 (0.7)	-0.062 (0.3)	0.5
Androgenic steroids	0.036 (0.2)	0.011 (0.8)	0.0029 (1)	0.14 (0.09)	0.092 (0.1)	
Androgenic steroids; Pregnenolone steroids; Progestin steroids	-0.031 (0.3)	-0.078 (0.2)	0.067 (0.2)	-0.054 (0.5)	-0.11 (0.07)	-1.0
		Digit :	Span Forw	/ard		

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# 3e) Attention and concentration domain (digit span backward test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r(P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r (P)	
Lysophospholipid; Phosphatidylethanolamine (PE); Phosphatidylcholine (PC); Monoacylglycerol; Diacylglycerol	-0.025 (0.4)	-0.11 (0.06)	-0.06 (0.2)	-0.089 (0.3)	0.21 (0.001)	1.0
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.042 (0.2)	-0.077 (0.2)	-0.15 (0.001)	-0.023 (0.8)	0.2 (0.001)	
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.042 (0.1)	-0.04 (0.5)	-0.015 (0.7)	-0.031 (0.7)	-0.1 (0.1)	- 0.5
Sphingolipid metabolism	1.7e-05 (1)	9e-04 (1)	0.019 (0.7)	-0.027 (0.7)	-0.028 (0.7)	
Primary bile acid metabolism; Secondary bile acid metabolism	-0.037 (0.2)	-0.096 (0.08)	0.038 (0.4)	-0.061 (0.5)	-0.0064 (0.9)	
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism, Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	-0.0064 (0.8)	-0.023 (0.7)	0.035 (0.5)	0.02 (0.8)	-0.088 (0.2)	- o
Food component/Plant	-0.017 (0.6)	-0.045 (0.4)	0.024 (0.6)	-0.057 (0.5)	-0.0072 (0.9)	0.5
Androgenic steroids	0.044 (0.1)	0.068 (0.2)	-0.025 (0.6)	0.098 (0.2)	0.13 (0.04)	
Androgenic steroids; Pregnenolone steroids; Progestin steroids	-0.01 (0.7)	-0.013 (0.8)	0.0039 (0.9)	-0.053 (0.5)	0.023 (0.7)	1.0

Digit Span Backward

# 3f) Ability to decode domain (word reading test)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r (P)	White Male r (P)	White Female r (P)	Black Male r (P)	Black Female r(P)				
Lysophospholipid; Phosphatidylethanolarnine (PE); Phosphatidylcholine (PC); Monoacylglycerol; Diacylglycerol	-0.048 (0.1)	-0.1 (0.07)	-0.079 (0.09)	-0.074 (0.4)	0.12 (0.05)	1.0			
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.041 (0.2)	-0.03 (0.6)	-0.072 (1)	-0.079 (0.3)	0.049 (0.4)				
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	-0.026 (0.4)	-0.054 (0.3)	-0.0048 (0.9)	0.068 (0.4)	-0.089 (0.2)	- 0.5			
Sphingolipid metabolism	0.0037 (0.9)	-0.069 (0.2)	0.044 (0.4)	0.047 (0.6)	-0.017 (0.8)				
Primary bile acid metabolism; Secondary bile acid metabolism	-0.0093 (0.8)	0.00092	0.062 (0.2)	-0.099 (0.2)	0.033 (0.6)				
Methionine, cysteine, SAM and taurine, polyamine Metabolism, Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	-0.028 (0.3)	-0.035 (0.5)	0.031 (0.5)	-0.052 (0.5)	-0.048 (0.4)	<b>-</b> 0			
Food component/Plant	-0.031 (0.3)	-0.11 (0.04)	-0.0033 (0.9)	-0.0 <b>4</b> 6 (0.6)	0.068 (0.3)	0.5			
Androgenic steroids	0.044 (0.1)	0.073 (0.2)	0.014 (0.8)	0.1 (0.2)	0.022 (0.7)				
Androgenic steroids; Pregnenolone steroids; Progestin steroids	-0.036 (0.2)	-0.051 (0.4)	-0.052 (0.3)	0.018 (0.8)	-0.0067 (0.9)	-1.0			
Word Reading									

# 3g) Executive function domain (trail making test B)

Sub-pathways representing most highly correlated metabolites (r>0.7)	Overall r(P)	White Male r (P)	White Female r(P)	Black Male r (P)	Black Female r (P)	
$Ly sophospholipid; Phosphatidylethan olamine (PE); Phosphatidylcholine (PC); \\ Monoacylglycerol; Diacylglycerol$	0.026 (0.4)	-0.02 <b>1</b> (0.7)	0.1 (0.03)	-0.03 (0.7)	-0.03 (0.6)	1.0
Fatty acid metabolism (acyl choline); Lysophospholipid	-0.0095 (0.7)	0.042 (0.5)	0.03 (0.5)	-0.13 (0.1)	-0.05 (0.4)	
Long chain fatty acid; Polyunsaturated fatty acid (n3 and n6); Fatty acid, monohydroxy; Fatty Acid, branched; Medium chain fatty acid; Endocannabinoid	0.026 (0.4)	0.076 (0.2)	0.031 (0.5)	0.03 (0.7)	-0.044 (0.5)	- 0.5
Sphingolipid metabolism	-0.0058 (0.8)	0.026 (0.6)	-0.021 (0.7)	-0.16 (0.05)	0.073 (0.2)	
Primary bile acid metabolism; Secondary bile acid metabolism	0.074 (0.01)	0.022 (0.7)	0.1 (0.03)	0.12 (0.1)	0.087 (0.2)	
Methionine, cysteine, SAM and taurine, polyamine Metabolism; Tryptophan, tyrosine, lysine, histidine metabolism, and other amino acid; Aminosugar, pentose metabolism, and other carbohydrate; Ascorbate and aldarate, and tocopherol metabolism; Purine and pyrimidine Metabolism; Acetylated peptides; Mevalonate metabolism, fatty acid, dicarboxylate, and androgenic steroids; Food component, benzoate metabolism, and other xenobiotics	0.064 (0.03)	-0.01 (0.9)	0.14 (0.004)	0.12 (0.2)	0.086 (0.2)	- 0
Food component/Plant	0.023 (0.4)	0.029 (0.6)	0.0099 (0.8)	0.043 (0.6)	0.021 (0.7)	0.5
Androgenic steroids	-0.013 (0.7)	-0.031 (0.6)	-0.0045 (0.9)	0.091 (0.3)	-0.093 (0.1)	
Androgenic steroids; Pregnenolone steroids; Progestin steroids	0.044 (0.1)	0.027 (0.6)	0.083 (0.08)	0.13 (0.1)	-0.078 (0.2)	-1.0

Trail Making Test B

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