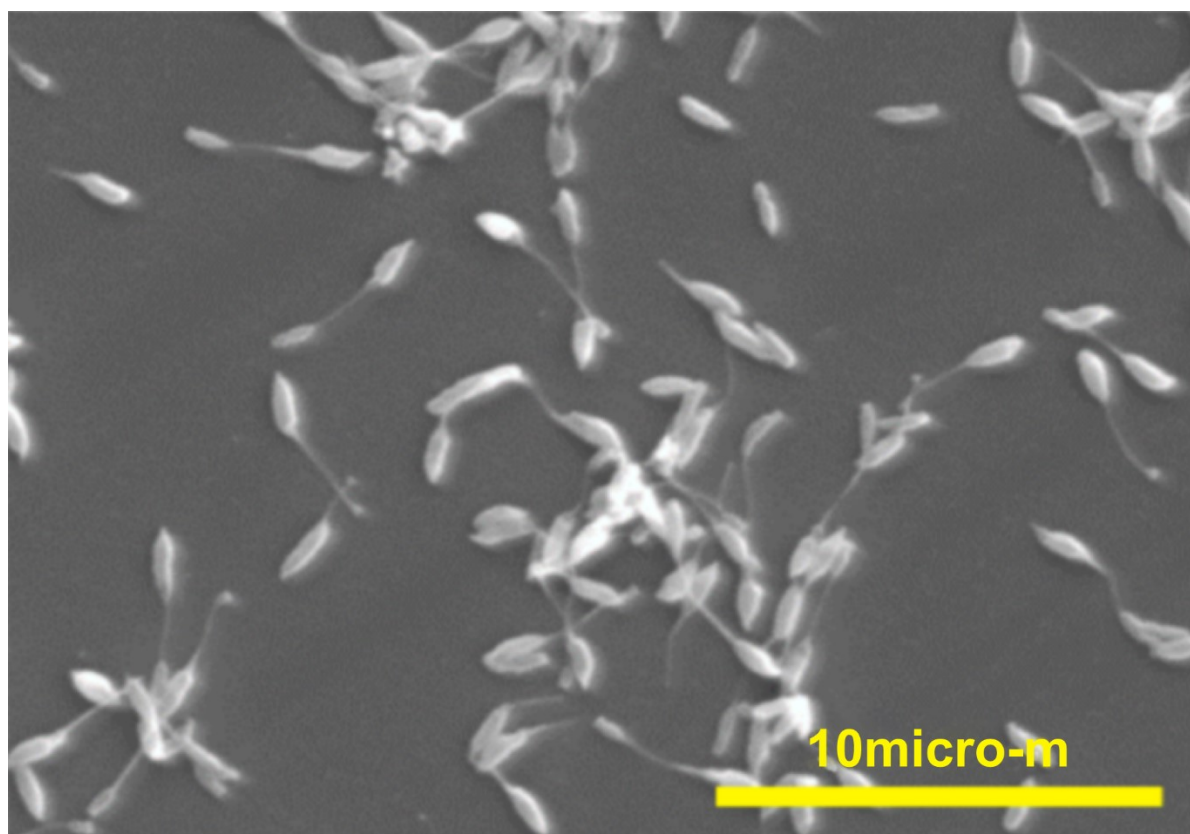
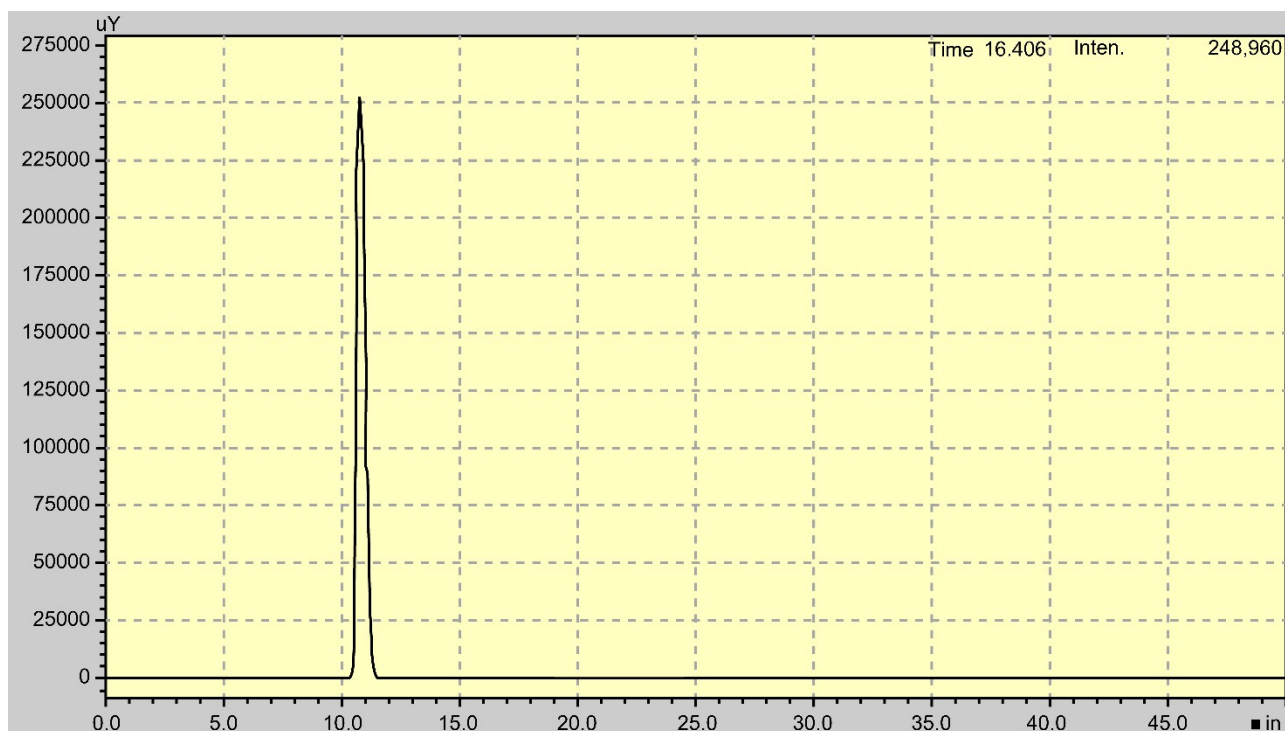


Supplementary Materials



Supplementary Figure S1. Scanning electron microscopy image of pyrroloquinoline quinone-producing bacteria

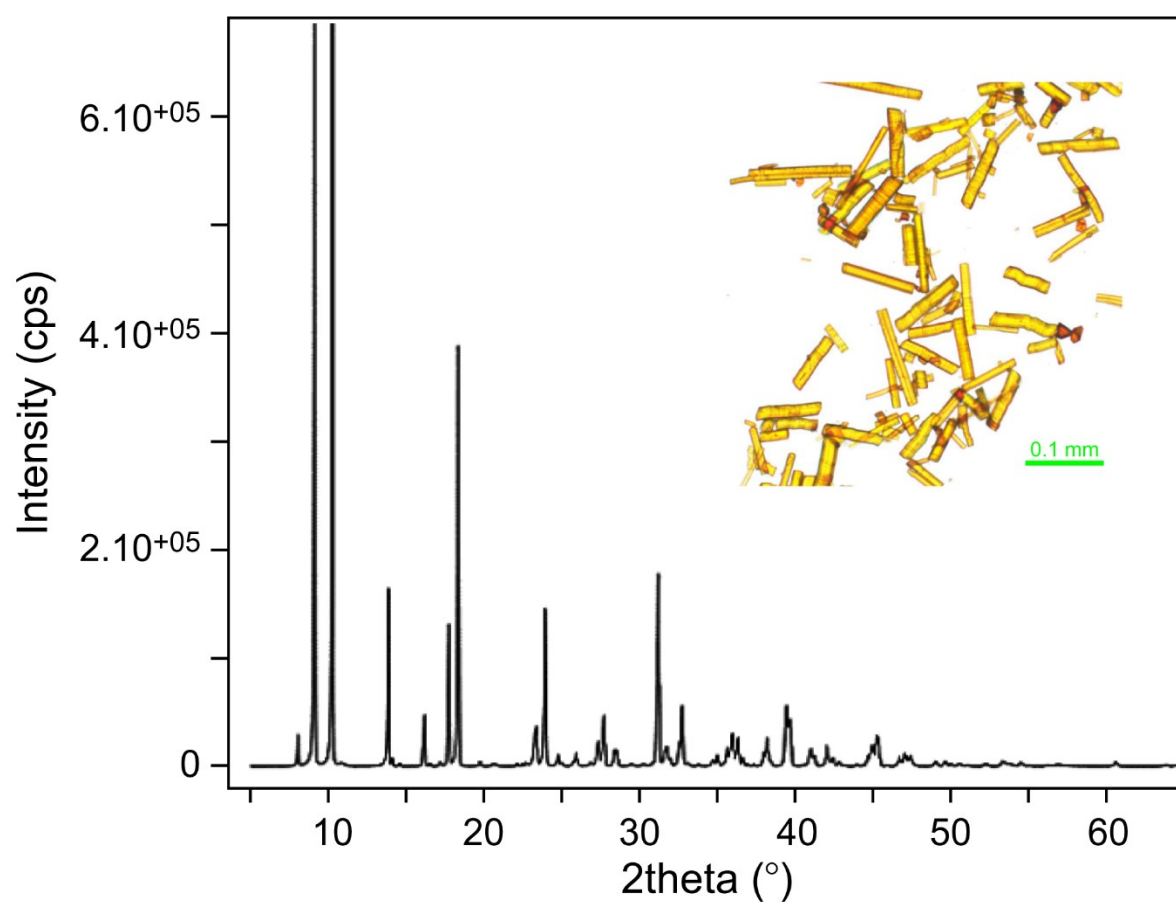


Supplementary Figure S2. HPLC chromatograph of pyrroloquinoline quinone disodium. The

product had high purity. HPLC condition: Detector UV 259 nm, Temperature 30°C TCI

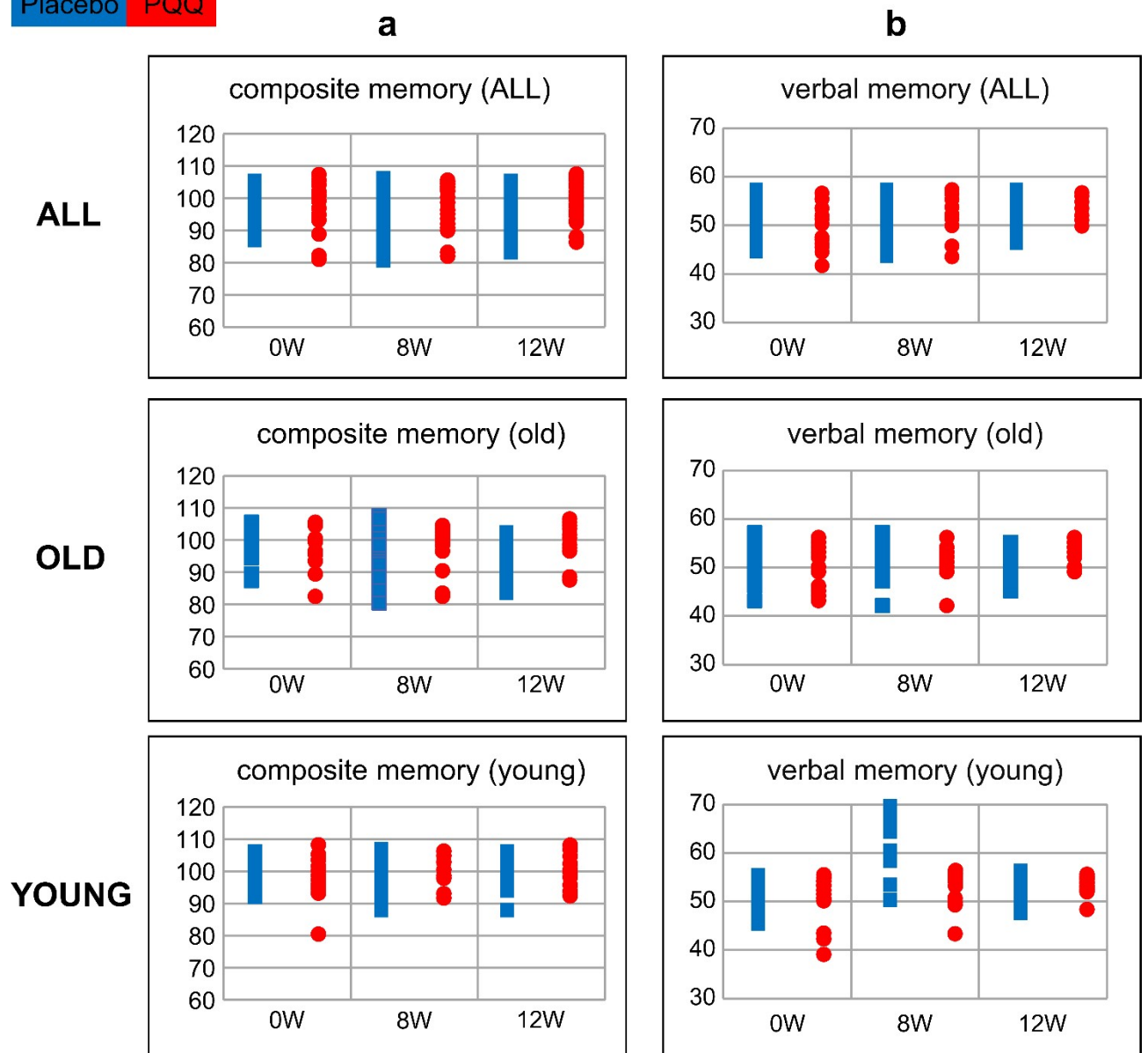
Kaseisorb LC 2000 150 mm x Φ 4.6 mm, 5 mm. A: 10 mM K_2HPO_4 /15 mM TBAB (pH 7.4) B:

acetonitrile A: B = 72:28



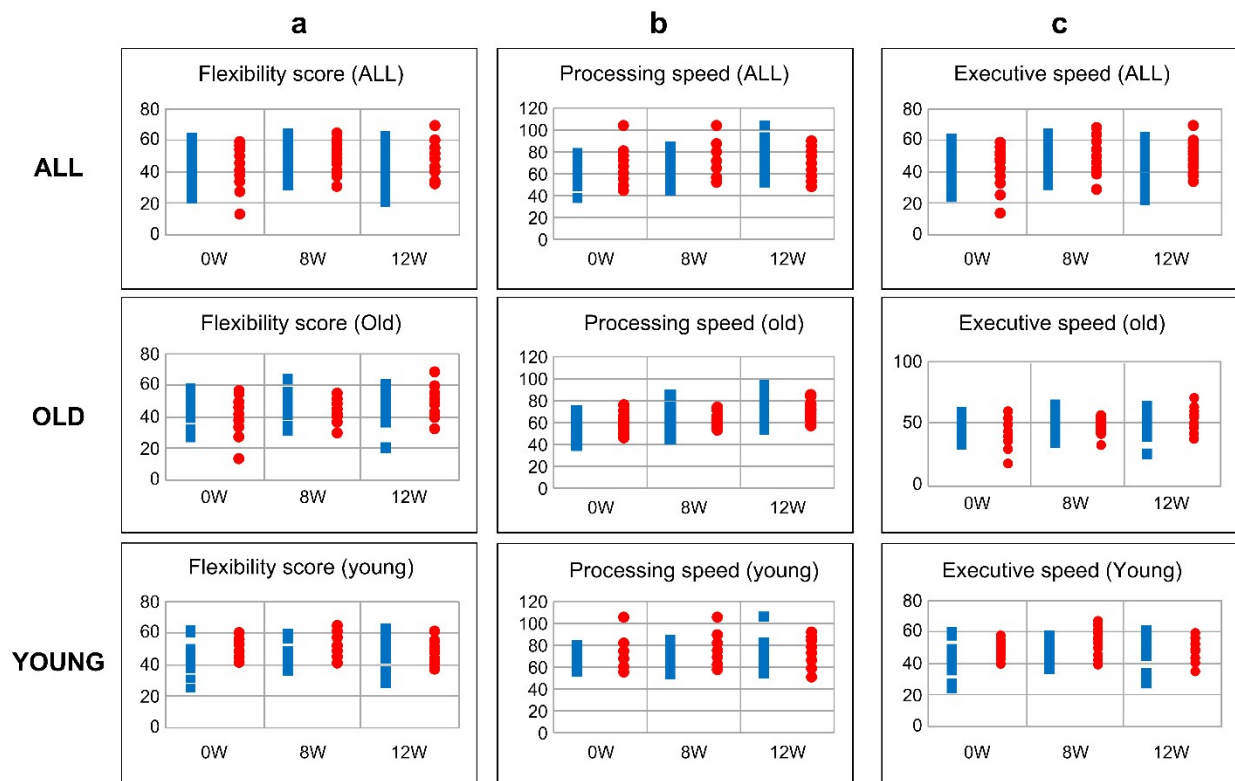
Supplementary Figure S3. X-ray diffraction (XRD) patterns of pyrroloquinoline quinone disodium trihydrate (PQQ). PQQ crystals were identified using X-ray diffraction analysis. Cu(K-beta) 45 kV 200 mA

Placebo PQQ



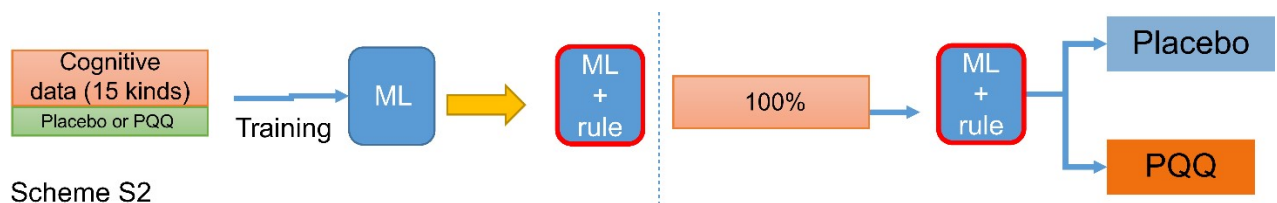
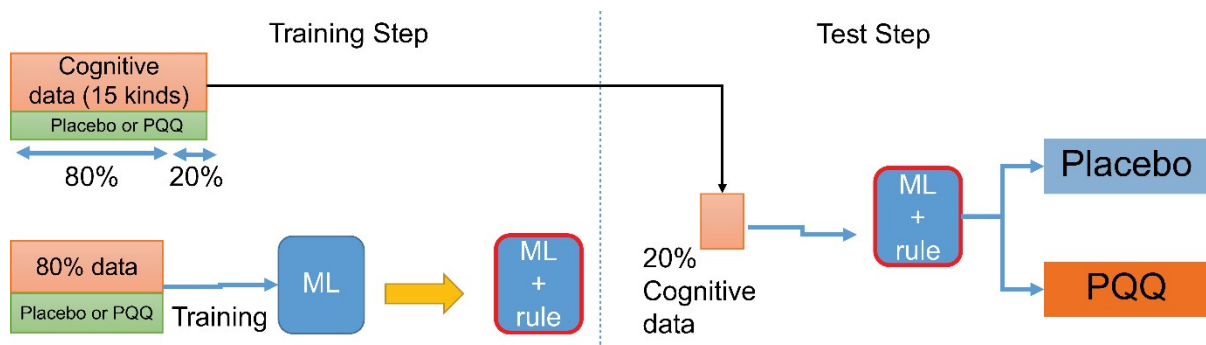
Supplementary Figure S4. Dot plot graph: Blue indicates the placebo. Red indicates PQQ.

Composite memory (a) and verbal memory (b) scores.



Supplementary Figure S5. Dot plot graph: Blue indicates the placebo. Red indicates PQQ.

Cognitive Flexibility (a), processing speed (b), and executive speed (c) scores



Scheme S2

Scheme Experimental method of machine learning (logistic regression)

The training data associates whether they belong to the PQQ group or the placebo group. Judgment (PQQ or placebo) is made using only cognitive data.

S1: We trained with 80% of the data and confirmed the judgment rules with the results of the cognitive test of 20%.

S2: We trained on all the data. Judgment rules were confirmed for all cognitive test results.

Scheme. Scheme Experimental method of machine learning (logistic regression). The training data associate whether the participants belong to the PQQ group or placebo group. Judgment (PQQ or placebo) is made using only cognitive data. S1: We trained with 80% of the data and confirmed the judgment rules with the results of the cognitive test of 20%. S2: We trained all data. Judgment rules were confirmed for all cognitive test results.

Supplementary Table S1. Cognitive test results for all participants

Function	Group	0 week (average)	0 week (SD)	8 week (average)	8 week (SD)	8w P value (A- B)	12 week (average)	12 week (SD)	12w P value (A- B)
Composite memory	Placebo(A)	98.161	4.981	97.871	6.994	0.349	96.194	5.695	0.003
	BioPQQ(B)	97.484	7.234	99.452	6.180		100.452	5.156	
Verbal memory	Placebo(A)	51.161	3.287	52.419	3.810	0.806	51.645	3.272	0.001
	BioPQQ(B)	51.000	4.531	52.645	3.392		54.097	2.271	
Visual memory	Placebo(A)	47.000	3.540	45.452	4.632	0.235	44.548	4.081	0.074
	BioPQQ(B)	46.484	4.024	46.806	4.246		46.355	3.747	
Psychomotor speed	Placebo(A)	185.548	18.854	189.387	17.285	0.283	190.258	17.405	0.491
	BioPQQ(B)	188.419	25.971	194.968	22.863		193.774	22.253	
Reaction time	Placebo(A)	661.355	69.333	673.097	69.288	0.174	643.677	69.157	0.663
	BioPQQ(B)	652.516	115.226	644.742	91.424		633.935	102.852	

Complex attention	Placebo(A) 5.645	3.322	5.387	3.490	0.445	5.871	4.209	0.371
	BioPQQ(B) 5.742	3.326	4.742	3.109		4.903	4.245	
Cognitive flexibility	Placebo(A) 44.710	9.303	47.355	8.110	0.174	48.516	9.241	0.143
	BioPQQ(B) 46.452	9.750	50.097	7.569		51.871	8.531	
Processing speed	Placebo(A) 62.613	8.831	63.677	9.167	0.047	68.000	9.324	0.248
	BioPQQ(B) 66.323	11.044	68.903	11.080		71.194	12.040	
Executive speed	Placebo(A) 45.774	8.995	48.419	7.784	0.138	49.613	9.084	0.144
	BioPQQ(B) 47.645	9.824	51.419	7.924		52.935	8.594	
Social acuity	Placebo(A) 6.935	2.874	7.065	2.620	0.408	6.935	2.909	0.070
	BioPQQ(B) 7.129	2.513	7.645	2.858		8.226	2.578	
Reasoning	Placebo(A) 6.032	4.317	5.806	4.102	0.297	7.710	3.926	0.635
	BioPQQ(B) 6.710	3.900	6.903	4.110		8.161	3.522	

Working memory	Placebo(A)	10.323	3.525	11.581	3.042	0.414	11.452	3.385	1.000
	BioPQQ(B)	11.097	3.673	12.194	2.822		11.452	3.974	
Sustained attention	Placebo(A)	30.839	4.525	33.323	3.219	0.720	32.581	4.493	0.958
	BioPQQ(B)	32.129	4.387	32.903	5.635		32.645	5.200	
Simple attention	Placebo(A)	39.710	0.588	39.581	0.886	1.000	39.065	1.999	0.858
	BioPQQ(B)	39.355	1.170	39.581	0.765		38.968	2.228	
Motor speed	Placebo(A)	122.129	13.766	124.645	13.212	0.861	121.258	13.518	0.950
	BioPQQ(B)	121.452	18.765	125.290	15.612		121.484	14.951	

Supplementary Table S2. Cognitive test results of the Old group

Function	Group	0 week (average)	0 week (SD)	8 week (average)	8 week (SD)	8w P value (A- B)	12 week (average)	12 week (SD)	12w P value (A- B)
Composite memory	Placebo(A)	97.833	5.628	96.778	7.628	0.812	94.333	5.477	0.011
	BioPQQ(B)	95.133	7.039	97.400	7.129		99.733	5.910	
Verbal memory	Placebo(A)	51.222	3.590	51.778	4.052	0.893	50.500	3.222	0.002
	BioPQQ(B)	50.533	4.324	51.600	3.312		53.800	2.210	
Visual memory	Placebo(A)	46.611	3.987	45.000	4.887	0.646	43.833	4.134	0.147
	BioPQQ(B)	44.600	3.738	45.800	5.003		45.933	3.918	
Psychomotor speed	Placebo(A)	181.222	19.408	186.333	17.409	0.410	186.889	16.799	0.283
	BioPQQ(B)	173.600	20.497	181.800	12.846		180.333	17.573	
Reaction time	Placebo(A)	681.944	57.556	681.056	66.453	0.962	662.667	55.890	0.649
	BioPQQ(B)	698.867	143.077	679.600	106.836		677.667	124.613	

Complex attention	Placebo(A) 4.444	2.995	4.056	2.754	0.741	5.000	3.865	0.934
	BioPQQ(B) 6.533	3.889	4.400	3.180		4.867	5.290	
Cognitive flexibility	Placebo(A) 45.389	7.755	48.611	8.233	0.400	47.778	10.103	0.859
	BioPQQ(B) 41.867	11.581	46.333	6.842		47.200	7.966	
Processing speed	Placebo(A) 60.333	8.575	62.333	9.356	0.847	64.944	7.596	0.512
	BioPQQ(B) 61.333	7.871	62.867	5.527		63.200	7.447	
Executive speed	Placebo(A) 46.278	7.387	49.556	8.046	0.405	48.611	9.960	0.882
	BioPQQ(B) 43.067	11.622	47.333	6.852		48.133	7.999	
Social acuity	Placebo(A) 6.611	2.933	6.889	2.610	0.981	6.444	2.572	0.125
	BioPQQ(B) 6.667	2.193	6.867	2.615		7.867	2.588	
Reasoning	Placebo(A) 6.500	4.592	6.111	3.496	0.538	7.333	3.144	1.000
	BioPQQ(B) 5.867	4.172	5.267	4.301		7.333	2.944	

Working memory	Placebo(A)	9.444	3.634	11.389	3.032	0.903	10.889	3.563	0.787
	BioPQQ(B)	10.133	4.307	11.267	2.604		10.533	3.925	
Sustained attention	Placebo(A)	29.778	4.346	33.000	3.254	0.350	32.111	4.185	0.938
	BioPQQ(B)	30.933	5.365	31.200	7.243		32.000	3.946	
Simple attention	Placebo(A)	39.833	0.383	39.667	0.594	0.455	39.278	1.841	0.544
	BioPQQ(B)	39.200	1.474	39.467	0.915		38.800	2.624	
Motor speed	Placebo(A)	120.056	13.901	123.167	12.249	0.231	121.000	13.447	0.293
	BioPQQ(B)	111.600	15.310	118.200	10.818		115.867	14.050	

Supplementary Table S3. Cognitive test results of the Young group

Function	Group	0 week (average)	0 week (SD)	8 week (average)	8 week (SD)	8w P value (A- B)	12 week (average)	12 week (SD)	12w P value (A- B)
Composite memory	Placebo(A)	98.615	4.093	99.385	5.966	0.317	98.769	5.118	0.195
	BioPQQ(B)	99.688	6.906	101.375	4.559		101.125	4.425	
Verbal memory	Placebo(A)	51.077	2.957	53.308	3.401	0.800	53.231	2.713	0.235
	BioPQQ(B)	51.438	4.816	53.625	3.263		54.375	2.363	
Visual memory	Placebo(A)	47.538	2.876	46.077	4.368	0.249	45.538	3.950	0.400
	BioPQQ(B)	48.250	3.531	47.750	3.276		46.750	3.661	
Psychomotor speed	Placebo(A)	191.538	16.974	193.615	16.860	0.090	194.923	17.802	0.106
	BioPQQ(B)	202.313	23.053	207.313	23.568		206.375	18.765	
Reaction time	Placebo(A)	632.846	76.212	662.077	74.294	0.056	617.385	79.006	0.333
	BioPQQ(B)	609.063	57.318	612.063	60.906		592.938	54.394	

Complex attention	Placebo(A) 7.308	3.119	7.231	3.655	0.096	7.077	4.518	0.145
	BioPQQ(B) 5.000	2.608	5.063	3.108		4.938	3.151	
Cognitive flexibility	Placebo(A) 43.769	11.381	45.615	7.922	0.006	49.538	8.181	0.021
	BioPQQ(B) 50.750	4.919	53.625	6.592		56.250	6.638	
Processing speed	Placebo(A) 65.769	8.497	65.538	8.922	0.034	72.231	10.109	0.109
	BioPQQ(B) 71.000	11.742	74.563	12.099		78.688	10.694	
Executive speed	Placebo(A) 45.077	11.139	46.846	7.426	0.004	51.000	7.885	0.024
	BioPQQ(B) 51.938	5.131	55.250	7.029		57.438	6.582	
Social acuity	Placebo(A) 7.385	2.844	7.308	2.720	0.326	7.615	3.305	0.396
	BioPQQ(B) 7.563	2.780	8.375	2.964		8.563	2.607	
Reasoning	Placebo(A) 5.385	3.990	5.385	4.942	0.059	8.231	4.902	0.669
	BioPQQ(B) 7.500	3.578	8.438	3.366		8.938	3.924	

Working memory	Placebo(A)	11.538	3.099	11.846	3.158	0.283	12.231	3.086	0.952
	BioPQQ(B)	12.000	2.805	13.063	2.816		12.313	3.945	
Sustained attention	Placebo(A)	32.308	4.516	33.769	3.244	0.534	33.231	4.986	0.993
	BioPQQ(B)	33.250	2.978	34.500	2.989		33.250	6.224	
Simple attention	Placebo(A)	39.538	0.776	39.462	1.198	0.515	38.769	2.242	0.644
	BioPQQ(B)	39.500	0.816	39.688	0.602		39.125	1.857	
Motor speed	Placebo(A)	125.000	13.589	126.692	14.699	0.384	121.615	14.157	0.341
	BioPQQ(B)	130.688	17.246	131.938	16.759		126.750	14.201	
