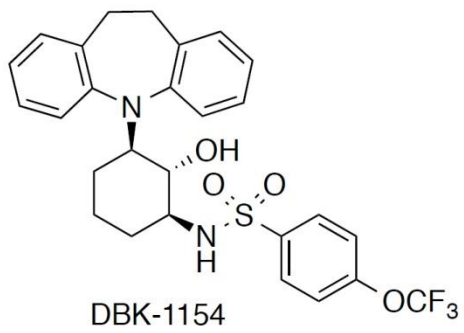
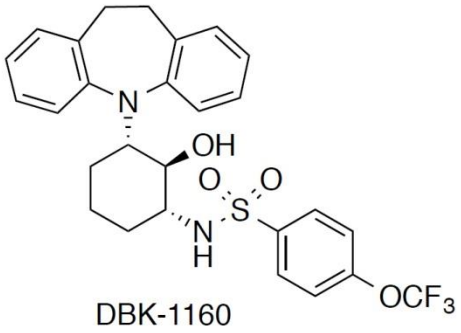
Supplementary Fig. 1 Chemical structures of DBK-1154 and DBK-1160



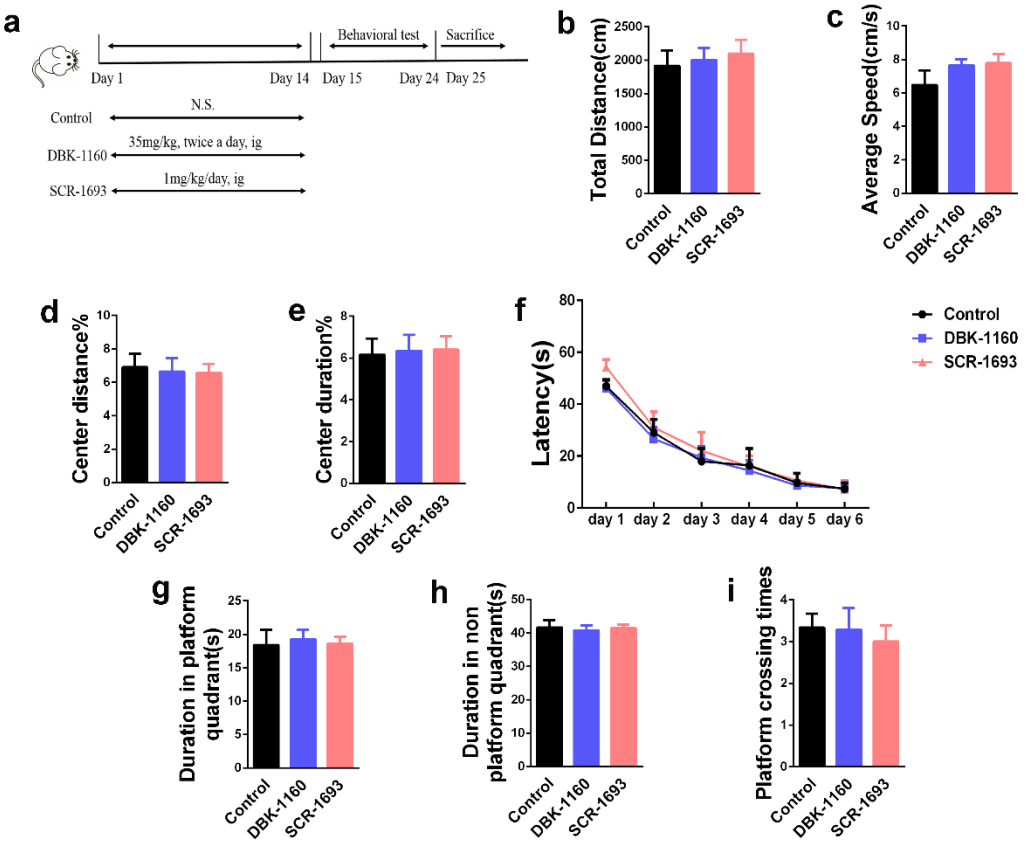
DBK-1154



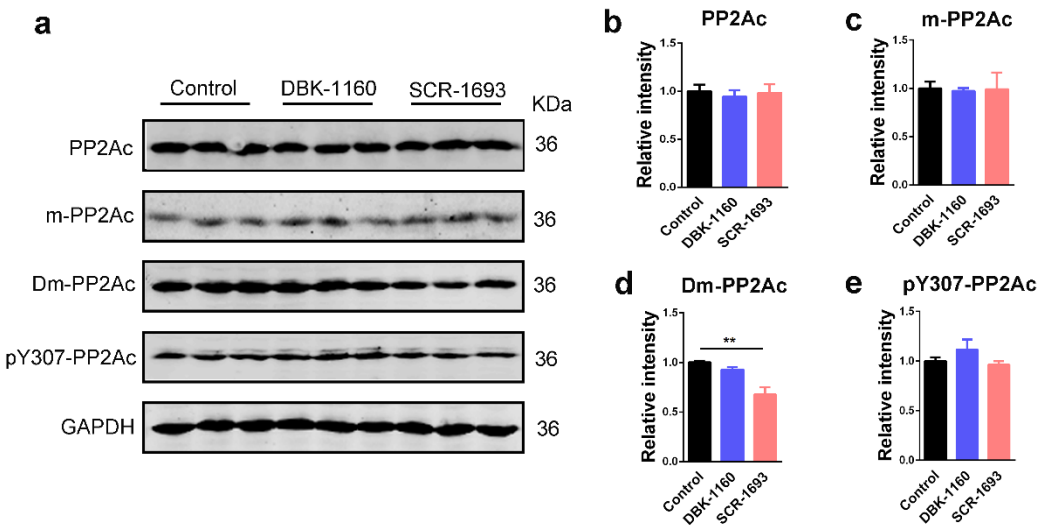
DBK-1160

Supplementary Table 1 Microsome Stability for DBK-1154 and DBK-1160

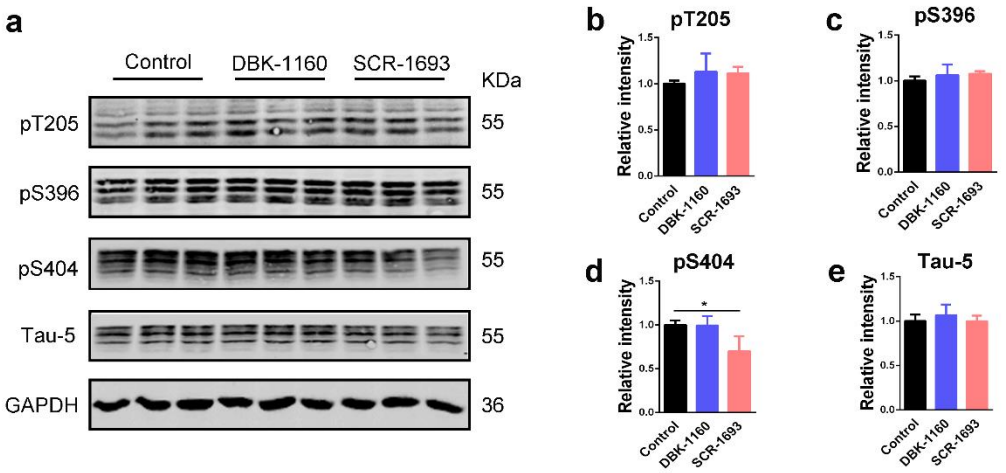
Species	**DBK-1154**			**DBK-1160**		
	$T_{1/2}$ min	% remaining at 60 min.	CLint mL/hr/kg	$T_{1/2}$ min	% remaining at 60 min.	CLint mL/hr/kg
human	13.5	3.7	237	26.6	17.7	121
rat	7.3	0.4	683	12.1	2.8	411
mouse	4.6	0.1	2363	9.0	1.3	1211



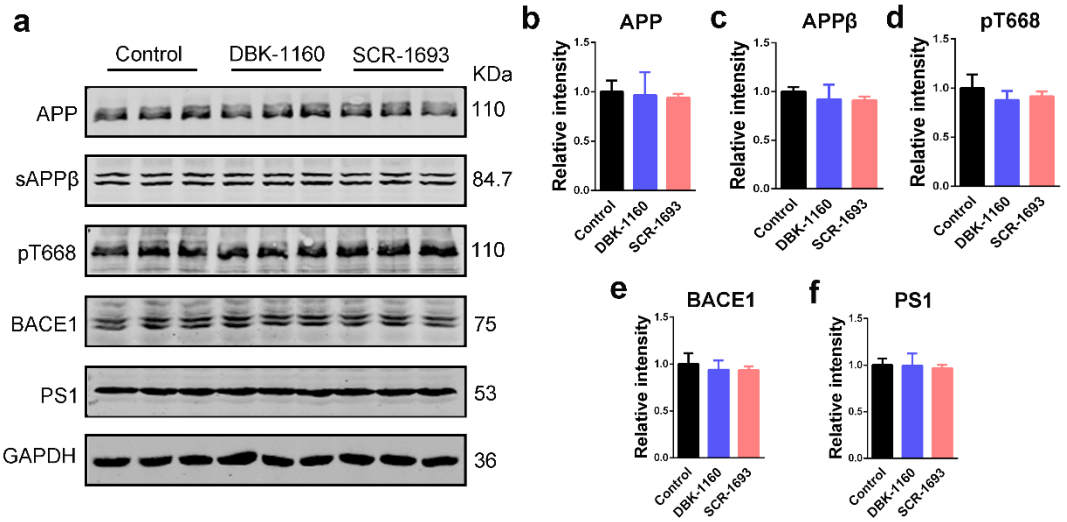
Supplementary Fig.2 DBK-1160 or SCR1693 treatment alone does not influence the general motor activity and cognitive function of normal rats. **(a)** Animal experiment timeline performed in the study. **(b-e)** The total distance, average speed, center distance/total distance and center duration/total duration were analyzed in the open field test. **(f)** Escape latency in six days were analyzed in the Morris water maze (MWM). **(g-i)** The duration in platform quadrant and non-platform quadrants, as well as platform crossing times on test day were analyzed in MWM. Data represent mean ± SEM, Control group (treated with normal saline) n=6, DBK-1160 group (treated with DBK-1160) n=7, SCR-1693 group (treated with SCR-1693) n=7



Supplementary Fig.3 DBK-1160 treatment alone does not change the post-translational modifications and activities of PP2A in normal rats. **(a)** Western blots for the catalytic subunit of PP2A (PP2Ac), methylated PP2Ac (m-PP2Ac), demethylated PP2Ac (Dm-PP2Ac) and phosphorylated PP2Ac at Y307 (pY307-PP2Ac) in rat hippocampus. **(b-e)** Quantification of the relative protein levels (PP2Ac, m-PP2Ac, Dm-PP2Ac and pY307-PP2Ac) after normalization to the GAPDH signal. Data represent mean ± SD, n=3, $^{**}P < 0.01$



Supplementary Fig.4 DBK-1160 treatment alone has no effect on tau phosphorylation in normal rats. **(a)** Western blots for tau phosphorylation levels at the sites of pT205, pS396, pS404 and total tau (Tau-5) in rat hippocampus. **(b-e)** Quantification of the relative protein expression levels (pT205, pS396, pS404, and Tau-5) after normalization to the GAPDH signal. Data represent mean ± SD, n=3, **P*< 0.05



Supplementary Fig.5 DBK-1160 treatment alone does not change APP, BACE1 and PS1 expression and APP-T668 phosphorylation in normal rats. **(a)** Western blots for APP, sAPPβ, pT668APP, BACE1 and PS1 in rat hippocampus. **(b-f)** Quantification of the relative protein levels (APP, sAPPβ, pT668APP, BACE1 and PS1) after normalization to the GAPDH signal. Data represent mean ± SD, n=3