Fig. 4

Advanced paternal age confers autism susceptibility and also is a risk factor for other neurodevelopmental disorders. To combine *Tsc2* haploinsufficiency with advanced paternal age in mice, we bred old *Tsc2*$^{+/-}$ males with WT females and generated controls by crossing young *Tsc2*$^{+/-}$ males with WT females and assessed social behavior in the adult offspring. *Tsc2*$^{+/-}$ and WT offspring of both young and old fathers showed normal social approach behavior. Plotted is the time (s) test subjects spent exploring either a cage containing a conspecific (social cage) or an empty cage. * $P < 0.05$, ** $P > 0.01$. Data represent means +/- S.E.M.

Table 1

First trimester (*n*)	**Second trimester (*n*)**	**Third trimester (*n*)**	**Outside gestation (*n*)**	**χ^2**	***P***
Tuberous sclerosis and ASD					
47	57	75	51	7.983	0.0463*
Tuberous sclerosis, no ASD or other neurodevelopmental phenotypes					
67	74	58	66	1.943	0.5843
ASD, no tuberous sclerosis					
1741	1687	1606	1700	5.701	0.1271

The table shows the number of cases (*n*) in which peak seasonal flu activity coincided with the first, second or third trimester of gestation or was outside gestational periods. Data are shown for TSC individuals affected by ASD (tuberous sclerosis and ASD), TSC individuals unaffected by ASD or other neurodevelopmental phenotypes (tuberous sclerosis, no ASD or other neurodevelopmental phenotypes) and ASD cases unrelated to tuberous sclerosis (ASD, no tuberous sclerosis), along with results from the corresponding chi square analyses. * $P < 0.05$

Supplementary Table 1

	TSC & ASD	**TSC, no ASD, no ID, no IS**
Year of birth (Mean +/- S.D.)	1988 +/- 11 years	1986 +/- 16 years
Gender		
Male	50.87%	42.21%
Female	49.13%	57.79%
Intellectual disability		
Yes	90.87%	0%

No	6.52%	100%
Information not available	2.61%	0%
History of infantile spasms		
Yes	38.26%	0%
No	11.30%	100%
Information not available	50.43%	0%
Mutation		
TSC1	1.74%	8.30%
TSC2	18.26%	19.72%
Variant of unknown significance	0%	1.73%
No mutation identified	2.17%	6.23%
Data not available	77.83%	64.01%

The table shows details regarding the TSC clinical samples used for the current analysis. Information regarding year of birth, gender, clinical features (intellectual disability, history of infantile spasms) and mutational status are presented. TSC & ASD: TSC individuals affected by ASD; TSC, no ASD, no ID, no IS: TSC individuals not affected by ASD, intellectual disability or infantile spasms.