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Contents

#### 1 Abstract

Results from testing an impressive 1280 compounds on the average life spans of 126,681 worms (C. elegans) were published in 2014[1].

Their good results for nortriptyline, minocycline and biogenic amines have been replicated in mammals. I replicated thousands of their worm calculations, and extended them to include maximum life span. Changes in the worms' average and maximum life spans are correlated.

# 2 Methods

# 2.1 Finding Mammal Experiments That Replicated Worm Results

The worm paper very reasonably suggests retesting its good compounds in mammals.

I checked my big spread sheet of life span experiments[2].

Nortriptyline[3], minocycline[4] and biogenic amines[5] also worked in mammals.

compound or	worm	mammal experiments							
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010055	in								
	average	subjects	effect on	reference	comment				
	life span	Sabjeets	life span	1010101100	comment				
		mouse model of	longer life	6					
nortriptvline	+21%	amyotrophic lateral	0						
	, , , ,	sclerosis							
		mouse model of	no effect	6					
		Huntington's disease							
		recent human stroke	50% less	7					
		victims	risk of						
			dying						
minoevelino	$\pm 20\%$	mouse model of	+13%	8					
mmocychne	$\pm 2570$	amyotrophic lateral	longer on						
		sclerosis	average						
		mouse model of	+12%	9					
		Huntington's disease	longer on						
			average	1.0					
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biogenic amines	+10% to		1 1.0	10	spermidine				
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promethazine	+32%	mouse model of	same or	6	putrobolillo				
Promotinazinio	10270	amyotrophic lateral	shorter life	0					
		sclerosis							
		male rats	+7%	13	oestrogens				
			longer life	_					
beta-Estradiol	+7%	female rats	+0.3%	13	oestrogens				
			longer life						
		men with previous	no effect	14	high dose				
		myocardial infarction			estrogen				
		men with previous	3%	14	low dose				
		myocardial infarction	increased		estrogen				
			risk of						
			dying						
		postmenopausal	2% to 18%	15	estrogen				
		postmenopausal women	2% to 18% less risk of	15	estrogen				

# 2.2 Replicating Worm Calculations

A worm researcher<sup>1</sup> very nicely shared their data.

It basically looks like...

	Α	в	C	D	E	F	G	Н	T B	E E	K	L	М	N	0
1	this data	set cont	ains all the	C. elegans lifespar	n experimer	nts that w	ent into the	e LOPAC paper		1		I			
2	plate	col	row	WellID	date	set	strain	Drug	conc	day	died	alive	class	action	selectivity
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4	10		1 C	01001CB102607	102607	В	N2	DMSO	33	3 1	8	1 10			1
5	10		1 E	01001EB102607	102607	В	N2	DMSO	33	3 2	8	1 1		10	0
6	10		1 C	01001CA102607	102607	A	N2	DMSO	33	3 2	8	1 0			
7	10		1 A	01001AA102607	102607	A	N2	DMSO	33	3 2	5	1 1			23
8	10		1 D	01001DD102607	102607	D	N2	DMSO	33	3 2	5	1 1			10
9	10		1 E	01001EC102607	102607	C	N2	DMSO	33	3 2	5	1 3			
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126681	5	5	9 E	00509EA102607	10260	7 A	N2	trans-Dehydroandrosterone	33	3	4	1 8	Hormone		Aldosteror
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126683	6	5	9 E	00509ED102607	10260	7 D	N2	trans-Dehydroandrosterone	33	3	1	1 9	Hormone	20	Aldosteror
126684															
126685															

Part of the raw-looking data

Through a process of coding<sup>2</sup>, trial and error, I replicated thousands of their calculations:



It's reassuring that the big worm researchers<sup>3</sup> correctly calculated thousands of numbers.

<sup>1</sup>Michael Petrascheck

<sup>2</sup>Computer programmers sometimes call software "code".

<sup>3</sup>There's a rum or that this paper might qualify me as a junior big worm researcher. (OK, I started the rum or. ;-) )

# 2.3 Extending Worm Calculations To Include Maximum Life Span

The original paper reported the effect of each compound on average life span.

That's good.

Another commonly reported statistic is how much maximum life span changes.

It's the age of the oldest of the old.

After I replicated their calculations of changes to average life span, I was confident I could match

- 1. data for animals receiving a certain compound to
- 2. corresponding data for their control animals

and could calculate maximum life spans the same way. So I did.

I considered how long the oldest 10% lived.

Changes in average and max life span are correlated.



#### Changes In Maximum Life Span For The 57 "Hit" Compounds Reported In The Original Paper

	Life Span					
	Average	num				
Compound/drug	increase	increase	p-value			
Demeclocycline bydrochloride	16%	4%	2E-02			
Doxycycline hydrochloride	18%	1%	1E-02			
Minocycline hydrochloride	29%	10%	5E-04			
3 4-Dichloroisocoumarin	13%	7%	8E-02			
Amovanine	330%	10%	2E-04			
Amozapine Doxazosin mesylate	15%	10%	2L-04 1E-02			
Guanahanz asatata	10%	10% 0%	2E-02			
Guanapenz acetate	1 5 0 /	970 70/	2E-08			
Noftopidil dibydrochlorido	1 / 0/	7 70	2E-01			
Nartopiuli dinydrochionde	210/	9% 6%	55-02			
(±) Ostaslathanin malaata	2170	070 1/10/	3E-03			
	3070 1/10/	1470	2E-04			
Chlorprothivene bydrochloride	1470	070	7E-04			
chlorprotnixene hydrochloride	3370	10%	7E-09			
Cistevelene meleete	50%	6% C0/	4E-04			
Cortexolorie maleate	11%	6% 100/				
Dinydroergocristine methanesulfonate	34%	10%	2E-06			
Loxapine succinate	43%	15%	6E-09			
Methylergonovine maleate	28%	8%	5E-03			
N-(2-[4-(4-Chlorophenyl)piperazin-1-						
yl]ethyl)-3-methoxybenzamide	35%	14%	3E-09			
Pergolide methanesulfonate	37%	13%	9E-04			
Propionylpromazine hydrochloride	20%	11%	4E-03			
Thioridazine hydrochloride	31%	10%	3E-05			
Loratadine	18%	4%	3E-01			
Oxatomide	25%	7%	2E-05			
Promethazine hydrochloride	32%	6%	3E-04			
PAPP/LY-165,163	33%	12%	3E-06			
Amperozide hydrochloride	38%	13%	2E-05			
BRL 15572	10%	4%	3E-03			
Dihydroergotamine methanesulfonate	24%	5%	3E-02			
Ketanserin tartrate	13%	2%	4E-01			
LY-367,265	34%	10%	7E-04			
Metergoline	23%	5%	2E-02			
Mianserin hydrochloride	32%	8%	8E-08			
Cinnarizine	15%	6%	2E-04			
Nicardipine hydrochloride	23%	13%	3E-06			
Nitrendipine	25%	10%	3E-04			
Hexahydro-sila-difenidol hydrochloride	15%	6%	4E-03			
BRL 50481	18%	9%	4E-06			
Trequinsin hydrochloride	27%	12%	2E-07			
Vinpocetine	15%	4%	4E-05			
Vincristine sulfate	12%	2%	2E-01			
AMN082	8%	5%	5E-02			
Eliprodil	16%	2%	8E-01			
(R,R)-cis-Diethyl tetrahydro-2,8-						
chrysenediol	7%	3%	4E-01			
Beta-Estradiol	7%	4%	8E-02			
Cyproterone acetate	23%	-3%	9E-02			
Danazol	13%	7%	8E-03			
Psora-4	42%	14%	7E-10			
Quinidine sulfate	12%	5%	7E-02			
4-Phenyl-3-furoxancarbonitrile	30%	9%	2E-03			
7-Cyclopentyl-5-(4-phenoxy)phenyl-7H-						
pyrrolo[2,3-d]pyrimidin-4-ylamine	11%	7%	2E-03			
Cyclosporin A	18%	9%	1E-02			
DAPH	15%	7%	1E-01			
Kenpaullone	27%	12%	1E-04			
LFM-A13	27%	12%	1E-07			
SU 4312	5%	11%	8E-06			
Tyrphostin AG 1478	11%	6%	6E-04			

# 3 Discussion

I read that all three of the compounds that worked in worms and mammals affect nerves. Nortriptyline is an antidepressant[3].

Minocycline evidently penetrates the central nervous system[4].

Biogenic amines include neurotransmitters[5].

Maybe neural control of aging is evolutionarily conserved between worms and mammals.

## 4 Conclusion

Nortriptyline, minocycline and biogenic amines extended the average life spans of worms and mammals. Changes in the worms' average and maximum life spans are correlated.

# 5 Funding

No money was involved.

I donated my time and skillz because I was interested, and it seemed worthwhile.

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