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Eric Le Bourg. Is lifespan linked with developmental viability in *Drosophila melanogaster*?. *Experimental Gerontology*, 2021, pp.111583. 10.1016/j.exger.2021.111583 . hal-03379491

HAL Id: hal-03379491

<https://hal.science/hal-03379491>

Submitted on 15 Oct 2021

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2 **Is lifespan linked with developmental viability**
3 **in *Drosophila melanogaster*?**
4

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11
12 **Abstract**

13 Long-lived lines of flies have been selected by reproduction at older ages and correlated
14 responses observed, and particularly whether development of flies was modified. Using these
15 selected lines or flies subjected to larval crowding or food restriction during development, two
16 studies have computed, among lines, a correlation between viability of eggs and larvae and mean
17 lifespan of adults: mean lifespan was longer when the viability was lower, showing a selection of
18 fittest flies. The present study correlates viability and mean lifespan observed during three decades
19 in a single wild-type strain. Contrary to the previous studies, a slight but not significant positive
20 correlation is observed, showing that lifespan can hardly increase when viability increases.
21 Therefore, it is not clear whether development and lifespan are linked, as hypothesised by some
22 authors.

23
24 **Key-words**

25 *Drosophila melanogaster* – lifespan – viability

26 **Introduction**

27 Three centuries ago, Buffon (1749) wrote that, among species, duration of development is
28 linked with lifespan. This idea has been confirmed by showing that species are spread on a
29 continuum (Stearns, 1983) with, on one side, short-lived species with a small body size, a short
30 gestation, maturing quickly, and giving birth at short intervals to many offspring (e.g. mice and
31 rats), and, on the other side, species with the opposite life-history strategy (e.g. elephants or
32 primates).

33 Regarding, within a species, the relationship between development and ageing, Lints (1988)
34 reviewed the developmental theory of ageing stating that “some genes affect both traits
35 pleiotropically, or that genes affecting both characters are closely linked”. Studies of Lints and Lints
36 (1971) making to vary environmental conditions during development of *Drosophila melanogaster*
37 flies seemed to confirm this statement, showing a negative relationship between growth rate of
38 larvae and lifespan, but Lints (1988) concluded that Economos and Lints (1984, 1986) eventually
39 showed that there was “an optimal growth rate on both sides of which lifespan decreased”.

40 In addition, many studies have selected long-lived lines of flies by reproduction at older ages
41 and observed correlated responses and particularly whether development was modified. Reviewing
42 studies measuring in long-lived and control lines developmental time and viability of flies, i.e. the
43 percentage of eggs reaching adulthood, Wit et al. (2013) reported that any outcome could be
44 observed. These results could allow to conclude that there is no clear link between development and
45 mean lifespan of flies, but the only study (Buck et al., 2000) that computed a correlation between
46 the viability and mean lifespan of selected lines seemed to point in another direction (Fig. 1). Buck
47 et al. (2000) reported that mean lifespan decreased when viability increased in the 65-90% range,
48 but did not indicate whether they used the longevity of males, females, or of both sexes combined.
49 In flies subjected to larval crowding or food restriction during development, Zwaan et al. (1991)
50 also reported a lower mean lifespan, in each sex, when viability increased in the 60-90% range. A
51 high viability means that most of larvae, even the poorly fit ones, reach the adult stage. These flies
52 could have a low lifespan and this could explain the negative relationship between viability and
53 mean lifespan of the lines. As emphasised by Zwaan et al. (1991), one can hypothesise that, “if
54 viability is decreased, only the fittest individuals survive to adults (viability selection) and this
55 increase in mean fitness becomes evident in increased adult longevity”.

56 Obviously, these studies do not show that, at the individual level, there is a link between
57 viability and lifespan because viability is measured in groups and not at the individual level. In
58 human beings, the developmental origins of adult health and disease (DOHaD) theory explains that
59 early life events, including in utero, can have major consequences in the adult and even at old age

60 (reviews in Vaiserman 2019).

61 The purpose of this paper is to confirm or not the results of Buck et al. (2000) and Zwaan et
62 al. (1991) by correlating viability and mean lifespan. The same wild-type strain was used during
63 three decades and viability was observed for the very rearing groups used to observe lifespan in
64 various experiments, all these groups living in very similar conditions, **by controlling the age of
65 parents and larval crowding. Eggs were transferred into vials, making possible to know the
66 viability, developmental duration of flies, and the sex-ratio. In addition, larvae developed without
67 larval crowding on a fresh medium, not used by other flies, and thus with no wastes of previous
68 larvae or flies. For instance, urea, a toxic waste of larvae, which decreases viability and increases
69 development duration (Botella et al. 1985), increases in crowded cultures (Henry et al. 2018). It has
70 been shown that males and females developing in larval crowding conditions that emerged 3 days
71 after the first ones had a lower weight and lifespan, and females had a lower fecundity measured
72 once at young age (Lushchak et al., 2019): in all experiments reported below flies emerged 9-10
73 days after egg-laying.**

74

75 **Material and methods**

76 The viability of the wild-type strain Meyzieu, caught at the end of the 1970s near the city of
77 Lyon (France) was observed from 1988 to 2016 at 25°C in nearly 800 weeks (see the whole results
78 in Le Bourg, 2021a). Groups with a very low viability (see Fig. 1 in Le Bourg, 2021a) were
79 however not used to observe lifespan. Flies used in the present article were the control groups of
80 several articles observing the effect of various factors on lifespan (Le Bourg, 2007, 2010, 2011,
81 2012, 2021b; Le Bourg and Lints, 1989; Le Bourg and Médioni, 1991; Le Bourg et al., 2000, 2002,
82 2015; Le Rohellec and Le Bourg, 2009), and were subjected to the very same rearing conditions
83 (see below). The mean viability in the present study was 74.42% (26 groups, range: 41.37-87.09%).
84 The mean lifespan of males was 46.09 ± 1.02 days (26 groups, range of means: 35.24-53.76 days),
85 and that of females 52.37 ± 1.27 days (only 25 groups, females being not used in one experiment,
86 range of means: 38.39-65.22 days). The number of harvested eggs in each group was in the 700–
87 2975 range. The number of flies in the longevity experiments was in the 40-130 range, depending
88 on experiments.

89 In order to obtain the parents of the experimental flies, flies were allowed to lay eggs for one
90 night in a bottle containing the medium (agar, sugar, corn meal and killed yeast) containing a mould
91 inhibitor (para-hydroxymethyl-benzoic acid) and enriched with live yeast at the surface of the
92 medium. This medium was used in all experiments. Flies emerging 9–10 days after egg-laying were

93 transferred to fresh bottles: they are the parents of the experimental flies. Experimental flies were
94 obtained as follows: eggs laid by ca. 5 day-old parents during one night on a Petri dish containing
95 the medium coloured with charcoal were transferred by batches of 25 into 80 ml glass vials. At
96 emergence, flies were transferred in groups of 15 virgin flies of the same sex into 20 ml polystyrene
97 vials. Flies lived at 25°C (LD: 12-12) at the Earth gravity level (1 g) and were transferred twice a
98 week to new vials. To sum up, all groups of flies of the strain used in this article were subjected to
99 the very same conditions. In such conditions, one can expect that viability and lifespan can vary
100 among groups of flies because of random variations, showing a relationship between these traits if it
101 indeed exists. However, a caveat is that, obviously, changes did occur between 1988 and 2016. The
102 stocks of agar, sugar, corn meal, killed yeast were renewed when they were exhausted, and new live
103 yeast was bought very often, as it cannot be used for a long time, even if kept at 4°C. In addition,
104 even if the temperature was always the same, different incubators could be used. Therefore, “very
105 same conditions” should not be understood as meaning that all things were equal for three decades,
106 but simply that care was taken to use similar rearing conditions: temperature, larval density, age of
107 parents of experimental flies, transfers to new vials.

108

109 **Results and discussion**

110 Figure 2 shows the relationship between viability and lifespan. In each sex, the correlation is
111 positive but not significant ($r = 0.371$, $n = 26$ in males, and $r = 0.282$, $n = 25$ in females). Pooling
112 the two sexes, as Zwaan et al. (1991) did, made it become just significant ($r = 0.283$, $p = 0.0440$, $n =$
113 51). These results thus show hardly a positive correlation between viability and mean lifespan, but
114 in no case that longevity increased when viability decreased, contrary to the results of Buck et al.
115 (2000) and Zwaan et al. (1991). However, a significant correlation was observed in this last study
116 only if both sexes were pooled, the effect being marginally significant in each sex (Fig. 1). The
117 present results show that viability does not help to predict lifespan of flies able to reach the adult
118 stage. Observing individual durations of development and lifespans could allow to know whether
119 development is linked to lifespan at the individual level, but a previous study of Mayer and Baker
120 (1984) only showed a negligible relationship between these traits in both sexes, if any.

121 One of the strengths of the present study is that viability and lifespan were observed on the
122 same groups and that the rearing conditions were the same for all groups during nearly three
123 decades. One could thus expect that variation of viability and lifespan is linked to random
124 environmental variation and possibly to genetic drift. For instance, larval crowding is not controlled
125 in the stocks of flies kept in bottles for years, if not decades, and this could have an effect on

126 lifespan. Lints et al. (1989) showed lifespan variations during a 4-year period in a single strain and
127 were unable to explain them. Could the discrepancy between the present results and those of Buck
128 et al. (2000) and Zwaan et al. (1991) be explained by the fact that these authors manipulated
129 developmental conditions, by modifying larval density or food quantity (Zwaan et al., 1991), or age
130 at reproduction (Buck et al., 2000)? Indeed, the procedure of the present article is similar to that of
131 Mayer and Baker (1984) who, “instead of perturbing the systems of development and aging, ...
132 attempted to observe them in a "free running" state by minimizing stresses known to influence the
133 duration of development or the length of imaginal life span”.

134 For the time being, it seems possible to conclude that, when flies develop in controlled
135 conditions, there is no clear relationship between viability and mean lifespan, but these results do
136 not allow concluding that there is not any link between development and ageing, particularly in
137 human beings.

138 In humans, one of the first studies showing the importance of early-life events was that of
139 Barker and Osmond (1986) who reported that the 1968-1978 ischaemic heart disease prevalence in
140 various sites of UK, differing by their wealth, was strongly linked to infant mortality in 1921-1925
141 in the same sites. Because both infant mortality in 1921-1925 and ischaemic heart disease
142 prevalence in the 1970s were higher in lower socio-economic groups, the authors suggested that
143 “the geographical distribution of ischaemic heart disease in England and Wales reflects variations in
144 nutrition in early life”. In a subsequent study, Osmond et al. (1993) showed that low birth weight is
145 linked to death from cardiovascular disease in both sexes. It is thus not surprising that women
146 suffering from the 1944 Dutch winter famine during their mid-to late gestation gave birth to low-
147 weight babies, and, in addition, that famine during early gestation, even if birth weight was normal,
148 was also associated with cardio-vascular disease at middle age (review in Preston et al., 2018) and
149 death rate in women, but not in men (van Abeelen et al., 2012). On the whole, early-life events, and
150 particularly foetal nutrition, can have long-lasting adverse consequences in humans (review in
151 Vaiserman et al., 2018) and results in animal models are not at variance (Tarry-Adkins and Ozanne
152 2017).

153

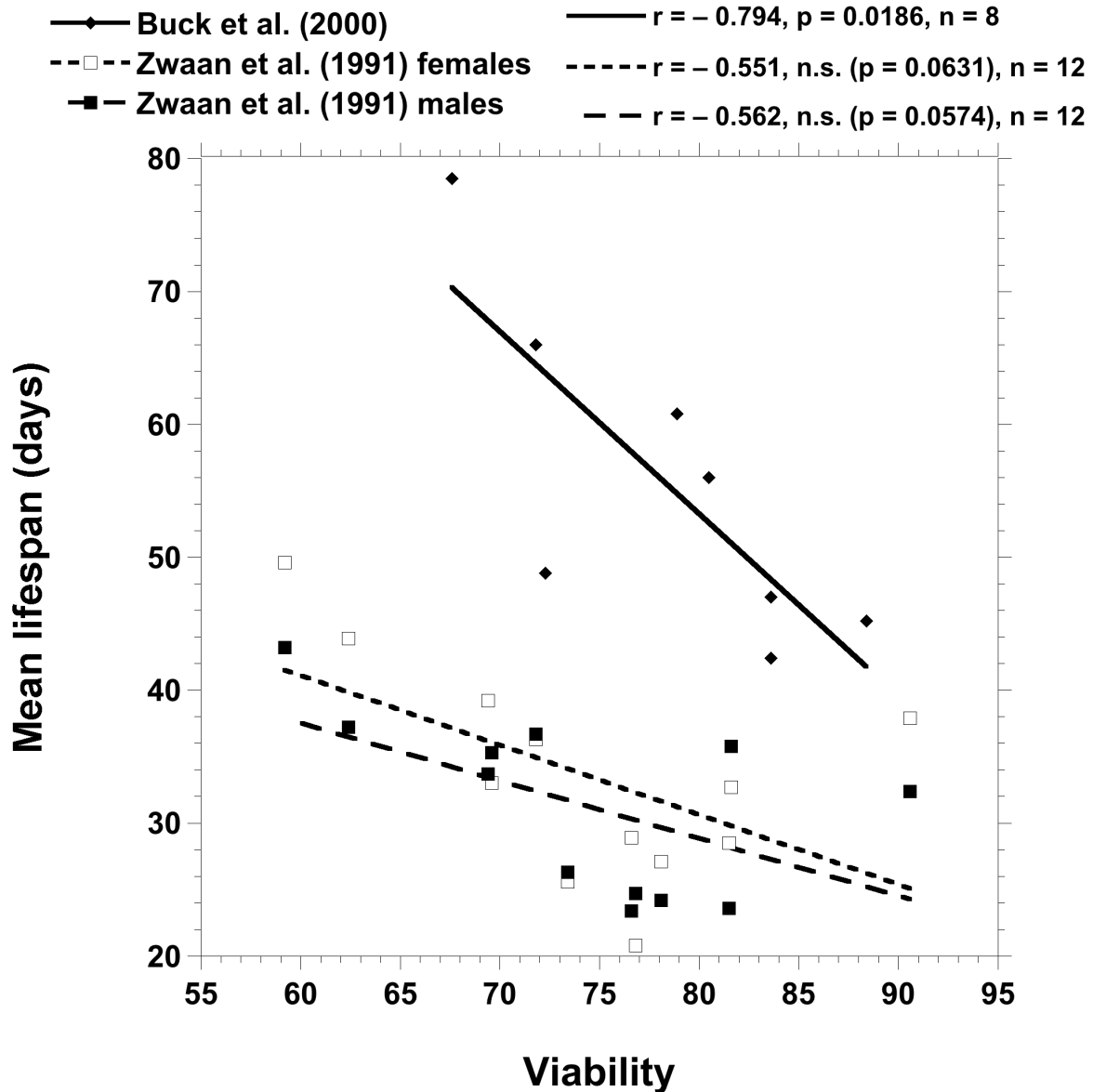
154 **Funding details**

155 This research did not receive any specific grant.

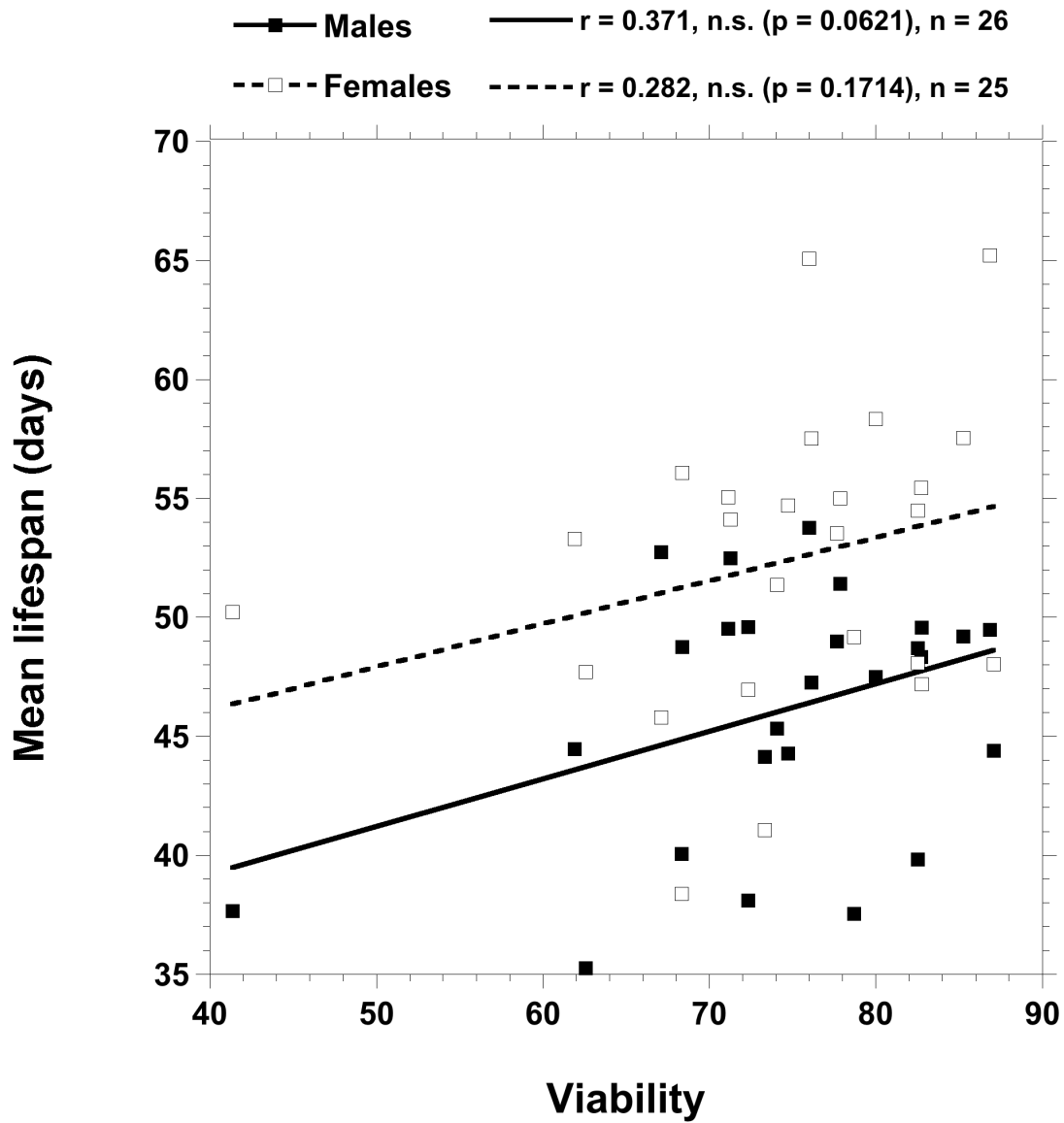
156 **Disclosure statement**

157 No conflict of interest.

158 Figure 1. Relationship between viability and mean lifespan in Buck et al. (2000) and Zwaan et
159 al. (1991). Lifespan is observed, respectively at 25 and 29°C, but the development is done at 25°C
160 in both studies. For the Buck et al.'s (2000) study, lifespan data were determined from Figure 5 and
161 viability ones were extracted from Table 2. For the Zwaan et al.'s (1991) study, data were extracted
162 from Tables 3, 4, 5, 7. The correlation is not significant in Zwaan et al. (1991) if sexes are analysed
163 separately, but the authors pooled sexes, which made the correlation being significant (in the figure:
164 $r = -0.546$, $p = 0.0057$, $n = 24$; in Zwaan et al. (1991): $r = -0.59$, $p < 0.01$). The correlation
165 reported by Buck et al. (2000) is $r = -0.791$ ($r = -0.794$ in the figure).



166 Figure 2. Relationship between viability and mean lifespan in the Meyzieu wild-type strain in
167 flies observed during three decades.



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