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The effects of individual housing on mice and rats: a review

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Abstract

Isolating an animal refers to the situation where the animal is physically fully demarcated from conspecifics without physical, visual, olfactory and auditory contact. Animals housed in separate cages in the same room are, although deprived of physical and visual contact, still in olfactory and auditory contact, and thus not totally isolated. During the fifties and sixties several studies claimed to show physiological and behavioural differences between individually and group housed rats and mice. The so-called 'Isolation Syndrome' characterised by changes in corticosterone levels, metabolism, growth, and behaviour was introduced, rather as a model for psychoneurosis than through any concern for animal welfare. Today, it is often stated as common knowledge in laboratory animal science textbooks that individual housing as well as isolation of rats and mice has an effect on physiology and behaviour. It is, however, unclear whether this effect actually impairs animal welfare.

The aim of this paper is to analyse studies on individual housing of mice and rats to evaluate whether there is documented proof that individual housing affects welfare, and, alternatively whether it is possible to house these animals individually without negative impact on welfare, eg by providing special housing improvements.

A range of studies have shown that individual housing or isolation has effects on corticosterone, the open field behaviour, barbiturate sleeping time and the metabolism of different pharmaceuticals in the animals. However, this review of 37 studies in rats and 17 studies in mice showed divergence in test results difficult to explain, as many studies lacked basal information about the study, eg information on genetic strains and housing conditions, such as bedding, enrichment and cage sizes. Furthermore, test and control groups most frequently differed in cage sizes and stocking densities, and behavioural tests differed in ways which may very well explain the differences in results. Overall, there seemed to be an effect of individual housing, although it may be small, and it seems reasonable to assume that, through making small changes in the procedures and housing environments, the effects can be minimised or even eliminated. More well-controlled and standardised studies are needed to give more specific answers to the questions this issue poses.

Keywords: *animal welfare, individual housing, isolation, mice, rats*

Introduction

During the fifties and sixties several studies claimed to show that individually housed mice and rats reacted physiologically and behaviourally different from group housed animals (Brain 1975). These observations led to the definition of the 'Isolation Syndrome' in mice and rats (Hatch *et al* 1965; Valzelli 1973) characterised by changes in corticosterone levels, metabolism, growth, and behaviour. Induction of the syndrome was introduced as a model for psychoneurosis rather than as a concern for animal welfare. Today it is considered common knowledge that individual housing or isolation of rodents has an effect on the animals' physiology and behaviour, and this is often stated in laboratory animal science textbooks: "Isolation of rats also appears to cause a stress reaction" (Svendsen 1994) and "Rats are social by nature, and an extensive literature shows that they are very sensitive to social isolation" (Koolhaas 1999), although not all textbook authors are that convinced about the impact of single housing: "The evidence suggesting that individual housing in mice can be deleterious is not convincing" (Baumans 1999).

The aim of this paper is to analyse studies on individual housing of mice and rats to evaluate whether there is documented proof that individual housing affects the welfare, alternatively whether it is possible to house these animals individually without negative impact on welfare, eg by providing special housing improvements.

Defining the terms

Often the terms single, individual or isolation housing are used indiscriminately. Isolating an animal refers to the situation during which the animal is physically fully demarcated from conspecifics without physical, visual, olfactory

and auditory contact, and few studies have been done on such animals. Animals housed in separate cages in the same room are, although deprived of physical and visual contact, still in olfactory and auditory contact, and thus not totally isolated. Moreover, when evaluating the effects on the animal, it might be useful to distinguish between individual housing, ie housing an animal alone at some time point, and individual rearing, ie individual housing of weanlings. Also, the term 'group-housed animals' can be defined differently. An animal in a group may react very differently depending on the group composition, size and density and each animals' position in the hierarchy etc. However, in the present paper, all group-housed animals will be referred to as such and any changes stated in individually housed or isolated animals are when compared to group housed animals unless otherwise stated.

The natural life of mice and rats

Generations of domestication may have evolved animals into laboratory animals, but when such individuals are placed in a complex and stimulating environment they will still show a rich variety of original behavioural patterns seen in the wild conspecifics (Smith *et al* 1994; Sluyter & van Oortmerssen 2000; Brain 1992; Holmes *et al* 2000; Barnett *et al* 1979; Berdoy 2002).

The wild rat

In the wild *Rattus norvegicus* is a ground-dweller. Its underground burrows contain long, branching tunnels, one or more exits and rooms for nests and food storage. In buildings rats are generally found in cellars, basements and lower floors. The social system is highly flexible (Lore & Flannelly 1977), but groups with one male are more successful. In a study of wild-caught rats kept in an inescapable enclosure, a parallel social system was demonstrated (Calhoun 1962). In one part of the enclosure higher ranking males established territories around burrows containing females. The dominant male excluded other males, and females within such a territory collectively nurtured their young. Such territorial colonies were reproductively successful with well-organised burrows and carefully maintained nests. Submissive males were forced together in large, non-territorial packs in which females were mated by several males and in which burrows were disorganised and reproduction was reduced, probably as a result of a high level of social stress.

The wild mouse

Wild-living populations of mice (*Mus musculus*) live in cracks in rocks or make complex burrows with numerous exits and chambers for nesting and food-storage (Berry 1970). The social system is highly flexible with a wide variety of social organisations depending on the environment (Brain 1989, 1992). Being highly territorial would not facilitate commensal living, as this often implies the exploitation of concentrated food sources, resulting in a high population density in a delimited area (Latham & Mason 2004). When living under commensal conditions mice are often both territorial and colonial (Mackintosh 1973; Poole & Morgan 1973, 1976). A dominant male sets up a territory with definite boundaries patrolled by frequently renewed scent marks, within which a family unit consists of the dominant male, several females and their pups and non-dispersing juveniles; a so-called deme (Latham & Mason 2004). However, there is some evidence that several males occasionally share a territory on an equal basis (Nowak 1999). Communal nesting defended by multiple mothers, also known from the laboratory mice, is thought to occur within some demes in commensal *M. musculus* (Hayes 2000; Manning *et al* 1995). In the wild, subordinate sexually mature mice move away from established territories to establish their own territories elsewhere (Latham & Mason 2004). During this dispersal phase, the animal lives alone. Some young mice remain non-territorial and such animals tend to be small (Latham & Mason 2004). Dispersing animals have been shown to have enlarged spleens and increased levels of adrenalin in the adrenals compared to dominant males (Thiessen 1966).

Both rats and mice are highly dependent on senses other than vision. Nevertheless the vision is fairly well-developed, even though the visual abilities of eg humans are far better. The sense of smell, hearing and touch are highly developed in mice and rats (Baumans 1999; Koolhaas 1999; Crawley 2000), and olfactory cues strongly determine the behaviour of these species. Olfactory cues are used eg to detect food, predators, territorial marks made by conspecifics, to identify the social status and sexual receptivity of conspecifics, and to select mates (Meikle *et al* 1995; Hurst *et al* 2001; Gosling *et al* 1996; Hurst 1990; Koolhaas 1999).

The use of sound is a major part of rat and mouse communication (Koolhaas 1999; Crawley 2000). Both species respond to a wide variety of ultrasonic signals between pups and parents and conspecifics such as distress calls. Ultrasonic signals vary in duration and range from 20 to 80 kHz in rats (Koolhaas 1999; Berdoy 2002) and 20 to 100 kHz in mice (Sales & Milligan 1992).

Effects of single housing and isolation on the animals

A range of studies have investigated the effects of individual housing or isolation on serum corticosterone, the open field behaviour, barbiturate sleeping time or the metabolism of various pharmaceuticals (Baer 1971).

Effects on corticosterone levels

The ultimate release of corticosterone into the bloodstream after stressor activation of the hypothalamic-pituitary-adrenocortical (HPA) axis is very sensitive and therefore the use of corticosterone for measuring stress has been frequently applied (Peng *et al* 1989; Sachser & Kaiser 1997; Tuli *et al* 1995).

In rats, a number of studies have been unable to reveal differences in corticosterone levels as a result of individual housing for periods between 3 weeks and 4 months (Gentsch *et al* 1981; Stern *et al* 1960; Viveros *et al* 1990; Holson *et al* 1991). Other studies, however, did show elevated levels after 5 – 26 weeks of individual housing (Plaut & Grota 1971; Greco *et al* 1989; Gamallo *et al* 1986),

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among these one study on rats individually housed in sound-proof boxes (Greco *et al* 1989). Another study showed a reduction in the level of corticosterone in isolated rats (Hurst *et al* 1997). Finally, in one study individual housing led to an increase in corticosterone in female rats and a decrease in males. The authors (Brown & Grunberg 1995) concluded the results could be explained by group-housed males trying to establish territories, whereas group-housed females cope by sharing distress with others. The same hypothesis is stated by Hurst *et al* (1997, 1998), but this does not explain the inconclusive observations on corticosterone in the above studies, the majority of which were conducted on males.

In mice, one study did show elevated levels of corticosterone after individual housing (Weltman *et al* 1968), but in a number of studies housing mice individually between 4 weeks and 6 months revealed no differences in corticosterone levels (Benton & Brain 1981; Goldsmith *et al* 1978; Misslin *et al* 1982).

The lack of changes in corticosterone for both rats and mice may indicate that being housed individually is not necessarily more stressful than being housed in groups, as being a part of a hierarchy may be very stressful, both when maintaining a position at the top of the hierarchy and when trying to get away from the bottom. The results presented above may, however, not be very useful for evaluating this issue, although changes in the corticosterone level is stated to be an important factor in the isolation syndrome (Hatch *et al* 1965; Valzelli 1973). Although common in welfare evaluations measuring corticosterone levels may be problematic for evaluating housing conditions (Krohn & Hansen 2002), as it is very sensitive and may be influenced by other factors, which may also be the reason for the multidirection in the corticosterone levels observed in individually housed mice and rats. Furthermore, a useful blood sample for corticosterone must be taken within a few minutes of the first disturbance to the animals, the time of day influences results, and corticosterone levels adapt under long term stress (Broom & Johnson 1993).

Effects on behaviour

The behavioural options often used to evaluate the effects of individual housing are various modifications of open field tests, which most frequently show an increased activity in individually compared to group-housed (Gentsch *et al* 1981; Gentsch *et al* 1982; Hall *et al* 1997a, b; Heidbreder *et al* 2000; Sahakian *et al* 1977; Holson *et al* 1988; Dalrymple-Alford & Benton 1981a,b).

In rats, a number of studies showed a reduction in exploration after individual housing (File 1978; Gamallo *et al* 1986), while a few others did not reveal any effects in any parameters (Einon *et al* 1981; Niesink & van Ree 1982). In another study, it was found that rats housed individually without visual contact with other rats for 21 days after weaning, had a reduced activity in the elevated plus maze and an increased avoidance of bright light (Stanford *et al* 1988).

In mice, some studies showed an increased open field activity after individual housing (Benton & Brain 1981; Goldsmith *et al* 1978; Weltman *et al* 1968; Faggin & Palermo-Neto 1985), while others revealed no such effects (Einon *et al* 1981; Rodgers & Cole 1993). In one study testing mice in the open field test for several days consecutively, the individually housed mice initially showed lower activity which, however, increased when they were habituated to the arena (Benton & Brain 1979).

Traditionally, exploration is seen as the animal being fit and able to deal with environmental challenges, and therefore it is interpreted as an indication of improved welfare (Walsh & Cummins 1976). Most frequently open field behaviour is referred to as ambulation or activity with no discussion of the ethological drive behind it. If ambulation or activity equals exploration, the conclusion would be that individual housing and isolation both have a positive effect on the animal's well-being. However, a high level of activity may also be flight motivated; the animal trying to escape the aversive arena (Barnett & Cowan 1976; Whimbey & Denenberg 1967). Another possible explanation of increased activity in individually housed or isolated animals is that due to the lack of home cage stimulation they are stimulated more when placed in new surroundings (Hall *et al* 2000). This makes it difficult to interpret and identify the drive behind the observations made in the various studies. An increase in self-directed behaviour, eg tail-chasing and self-grooming, has been observed in individually housed rats (Hurst *et al* 1997, 1998; Baenninger 1967). In general, stereotypic behaviour is seen in impoverished environments (Würbel *et al* 1998b), so individual housing may induce stereotypies, but actually no stereotypic behaviour was observed in the referred studies, either because it was not observed or because it was not registered. The absence of stereotypic behaviour may indicate a smaller welfare impact than is supposed from being housed individually. However, individual housing during the juvenile period leads to altered social skills when tested as adults (van den Berg *et al* 1999). In intruder tests, individually housed male mice display increased aggression compared to mice from group housed conditions. The younger the mouse when individual housing is initiated, the more aggressive it becomes (Cairns *et al* 1985). Male mice and rats housed individually for a period of time show more mounting and intromissions when re-housed with a female (de Catanzaro & Gorzalka 1980; Swanson & van de Poll 1983).

Looking at the animals' motivation to seek social company or preference for a cage containing conspecifics, does not show that social company is that important. In two studies on mice, the cage containing a partner was visited just as frequently as other cages containing food, space or shelter (Sherwin & Nicol 1996; Sherwin 1996). Also, the mouse preferred to rest in the cage containing the food rather than the social company, which may indicate, that the social companionship is not highly prioritised. An explanation of this could be that only visual contact between the two mice

was possible. In another study on rats, a rat could choose company in a T-maze and there was only a slight favour for the cage with conspecifics compared to an empty cage (Patterson-Kane *et al* 2001), although the rat could be in direct contact with the other rats.

Effects on metabolism

From pharmaceutical research and development it is well-known that housing conditions may influence the metabolism of different drugs (Baer 1971) and, in particular, barbiturate sleeping time in individually housed rodents has been extensively examined. Hormones (eg corticosterone and other stress hormones) are cleared from the blood through decomposition by the liver cytochrome P-450 complex, which also decomposes barbiturates and other foreign chemical components in the organism (Dairman & Balazs 1970). The amount of liver cytochrome P-450 complexes can be measured indirectly via the barbiturate sleeping time, which may be inversely correlated to stress (Lovell 1986b; Dairman & Balazs 1970). Therefore the more hormones the liver has to remove from the blood, the higher the amount of liver cytochrome P-450 complexes, and consequently the shorter the barbiturate sleeping time. In all studies, a reduced sleeping time was found for both individually housed mice and rats (Dairman & Balazs 1970; Einon *et al* 1976; Watanabe *et al* 1992). Analysing this reaction in detail showed altered pharmacokinetics in individually housed animals (Watanabe *et al* 1992).

A study on rats measuring plasma glucose and triglycerides showed significantly lower levels in individually housed rats, compared to group housed rats (Pérez *et al* 1997), showing that individual housing does cause variation in certain biochemical parameters.

Effects on neurochemistry and neural plasticity

Individually housed rodents have a decreased response to morphine (Kostowski *et al* 1977; Puglisi-Allegra & Oliverio 1983; Schenk *et al* 1987) and an increased pain threshold (Puglisi-Allegra & Oliverio 1983). The amphetamine-induced activity is higher in individually housed mice (Faggin & Palermo-Neto 1985; Wilmot *et al* 1986), and individually housed rats tend to increase self-administration of amphetamine (Schenk *et al* 1988). However, it is important to emphasise that this effect was non-significant. The mechanism behind the different reactions to different drugs is not revealed, which makes it difficult to interpret and conclude on the effects of housing conditions. However, increased administration of the dopamine agonist, amphetamine as well as decreased response to opioids may be correlated with changes in the dopaminergic activity of the brain as well as behavioural changes such as the appearance of stereotypies and the changed ambulation in the open field test (Robbins *et al* 1996; Steiner & Gerfen 1998). Dopamine agonists seem to intensify stereotypies, while antagonists, such as haloperidol, seem to dampen them (Ödberg 1984; Ödberg *et al* 1987). Endogenic opioids seem to be the inducers of stereotypies (Steiner & Gerfen 1998), and therefore it is reasonable to assume that animals with stereotypies metabolise opioids more rapidly.

Effects on growth and food intake

Individual housing may change feeding behaviour and, therefore, body weight and food consumption. Several studies, however, revealed no differences in body weight. In one study rats housed individually for 25 days had a lower body weight at the beginning of the study, but ended up with a higher body weight than group-housed rats (File 1978). In another study no effect on bodyweight was observed (Sobel *et al* 1979). For individually housed mice one study was unable to show any effect (Weltman *et al* 1968), whereas another study found a reduced body weight (Nagy *et al* 2002), and yet another study found an increased bodyweight (Takemoto *et al* 1975). Rats and mice are energy-consumers, and body weight is not likely to change as a result of individual housing, as the animals change their food consumption to keep the weight if required (Adolph 1947). Higher food consumption would be expected in individually housed animals due to the increase in space and the lack of heating from cage mates. However, one study found no differences in food consumption in neither rats (Szenasi *et al* 1988) nor mice housed individually (Takemoto *et al* 1975), while another study found a decreased food consumption (O'Connor & Eikelboom 2000) and yet two more studies found an increased food consumption (Brown & Grunberg 1996; Pérez *et al* 1997) in individually housed rats. Therefore, it is impossible to draw clear conclusions based on results from growth and food intake.

Effects on cardiovascular parameters

One study on mice (Spani *et al* 2003) and one on rats (Sharp *et al* 2003) revealed a higher heart rate in individually housed animals during the resting period, although the effect was not as distinct in rats as in mice. An increase in heart rate especially during resting periods may be interpreted as a symptom of stress (Krohn *et al* 2003). Three rat studies, one of which was performed on spontaneously hypersensitive rats, found no effects on blood pressure, when comparing individually housed rodents with group housed (Szenasi *et al* 1988; Hallback 1975; Sharp *et al* 2003).

Discussion

Scientific reasons may lead to individual housing of rodents, eg for metabolic and nutrition studies. A careful review of the literature, including 37 papers on rats (Table 1) and 17 papers on mice (Table 2) is, however, unable not only to clarify the impact of individual housing on animal well-being but also show how the eventual effects may be minimised. Only two studies were performed on isolated animals (Hurst *et al* 1997, 1998). Although 'isolation' is frequently used in paper titles, it almost always means individual housing, ie social physical isolation. So, it is impossible to compare the effects from isolation with the effects of individual housing to reveal any differences between the two housing types. Description of natural living makes it clear that vision is less important for both mice and rats, and the lack of visual contact with conspecifics cannot be regarded as isolation, in so far as contact remains through the primary sense of smell and hearing. Rats and mice

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respond equally to most parameters and do not seem to differ in their reaction to individual housing. 22% of the studies had the animals housed on grid floors, 22% housed them on various types of bedding, while in 56% of the studies flooring conditions were unclear. Being housed on grids could very well mask the effects of individual housing, depending on how stressful it is to be housed alone, as previous studies indicate that grid floor housing is stressful or at least unpleasant for rodents, and that it has major influence on behavioural and physiological parameters (Blom 1993; Manser *et al* 1996; Heidbreder *et al* 2000; Krohn *et al* 2003; Krohn & Hansen 2001). The great fluctuation in results of studies on individual housing may be due to some extent to differences in flooring conditions. In only one study was it stated explicitly that the animals were provided with enrichment in the form of paper towels and hay, whereas no enrichment was apparently given in the other 53 studies. Enrichment may have a great influence on the animal, and in a previous paper, the influence of enrichment on the brain is described and reviewed in detail (Mohammed *et al* 2002). Therefore it is very important to ascertain whether the animals have been enriched during the individual housing or not, as the effects of enrichment could be far stronger and noticeable than the effects of individual housing, at least when analysing the effects on the brain. When mice are group-housed in barren environments stereotypies may develop, which are, however, reduced by enriching the environment (Würbel *et al* 1998a). Placing an animal from a barren environment in an open field arena triggers explorative behaviour or curiosity (Zimmermann *et al* 2001; Schrijver *et al* 2002). Therefore, increased explorative behaviour is displayed by individually housed animals. This effect on the exploration behaviour might have been counteracted had the cages been extensively enriched; a point yet to be elucidated in any of the studies to date. In one study the isolation syndrome was easily obtained, but individually housed rats unfamiliar with the handler reacted with fear and freezing, while showing increased activity/exploration when familiar with the handler. In those instances where the open field arena was insufficiently cleaned between trials the first of the group-housed rats always reacted with fear and freezing, whereas activity and exploration were observed in those that followed (Holson *et al* 1991). Only 35% of the open field studies on individual housing state that they cleaned the arena between trials, whereas 65% state nothing about cleaning. In most of the rat studies, where the arena was known to be cleaned, individually housed rats showed higher activity, whereas only one study showed no effects on activity. These rats were, however, only individually housed for one week before testing. So, the use of an unfamiliar handler and the omission of cleaning the open field arena could lead to unclear results. Also, differences in cage sizes could play a significant role in behaviour and physiology, eg blood parameters, organ weights and social behaviour (McGlone *et al* 2001; Ödberg 1987; van Loo *et al* 2001). In the studies reviewed in this paper cage sizes seemed to be selected rather randomly. Individually housed rats were caged with a floor area ranging from 286 cm^2 to 1353 cm^2, while group-housed rats had floor areas from 930 cm^2 to 5625 cm^2 and stocking densities from 183 cm^2 to 948 cm^2 per animal. Individually housed mice were caged on floor areas ranging from 144 cm^2 to 830 cm^2, while group housed mice had floor areas from 360 cm^2 to 1445 cm^2 and stocking densities from 60 cm^2 to 210 cm^2 per animal. In only 30% of studies were the same cage sizes used for individually and group-housed animals, and in only one study (Takemoto *et al* 1975) was the same stocking density used for both. In all other studies no arguments were given for why cage sizes were chosen differently. One study on rats housed individually in differently sized cage revealed a direct correlation between cage size and activity in the open field (Syme & Hughes 1972), which is also the case for mice (Manosevitz & Pryor 1975). Whether or not the different cage sizes may have had an influence on the reviewed studies is unclear, but some of the discrepancies found may have been caused by different cage sizes as opposed to different housings.

Finally, different strains are known to react differently in behavioural and physiological tests (Cunliffe-Beamer *et al* 1981; Dahlborn *et al* 1996; Eskola & Kaliste-Korhonen 1998; Les 1968; Lovell 1986a; Nabeshima & Ho 1981; Schmitt & Hiemke 1998; File & Vellucci 1979; Gentsch *et al* 1981; van de Weerd *et al* 1994). Some strains may be very sensitive to individual housing, whereas others are unaffected (Vadiei *et al* 1990), and mice studied in open field tests and monitored for corticosterone levels may respond very differently when housed under different conditions (Krohn & Hansen 2002). Even rats of the same strain, but from different breeders show differences in behavioural and clinical chemistry (File & Vellucci 1979). Therefore, comparison of results from different studies on different strains is difficult. However, a number of different strains were used in these studies, and in all studies the information was incomplete, and full identification of the strain applied was impossible. In 24% of the studies it was even impossible to relate the strain used to either a commercial breeder or an in-house colony.

Animal welfare implications

Although the effects of individual housing have been an issue for the last forty years, it remains difficult to elucidate its impact on animal welfare. Today, there is no strong scientific basis for concluding that individual housing always imposes a major welfare problem in rats and mice, and more and better controlled studies are needed. Some previously monitored parameters, such as corticosterone levels, body weight, food consumption are very difficult or impossible to reach conclusions on as they are influenced by other factors. Although almost all studies reveal a significant difference in behaviour, biochemistry and pharmacology when comparing individually housed rats and mice with those that are group-housed (Table 1 and 2), they point in different directions. There probably is an effect of being housed individually, but the effect may not be that major, and it seems likely to assume that it could be eliminated or

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Table 1 Results from a literature review on individual housing of rats. Information about strain, sex, cage size and flooring conditions are given.

Strain	Sex	Cage size	Flooring conditions	Parameters	Analysis (Individual vs group)	Article
Unknown	F	Same size	Grid	Behaviour/social skills	Some significant diff.	(Baenninger 1967)
Wistar (CB)	M/F	Different size	Bedding	Corticosterone	Significant diff.	(Brown & Grunberg 1995)
Wistar (CB)	M/F	Different size	Bedding	Corticosterone/Feeding	Significant diff.	(Brown & Grunberg 1996)
Sherman (CB)	M	Different size	Grid	Barbiturate sleeping time	Significant diff.	(Dairman & Balazs 1970)
Lister Hooded (LB)	M/F	Different size	Unknown	Open Field test	Significant diff.	(Dalrymple-Alford & Benton 1981b)
Lister Hooded (LB)	M/F	Different size	Unknown	Open Field test	Significant diff.	(Dalrymple-Alford & Benton 1981a)
Sprague Dawley (CB)	M/F	Different size	Unknown	Barbiturate sleeping time	Significant diff.	(Einon *et al* 1976)
Lister Hooded (CB)	F	Different size	Unknown	Emergence test/Growth	Non-significant diff.	(Einon *et al* 1981)
Lister Hooded (CB)	M	Different size	Unknown	Object Contact test/Growth	Significant diff.	(File 1978)
Sprague Dawley (LB)	M	Different size	Unknown	Open Field test/Corticosterone	Significant diff.	(Gamallo *et al* 1986)
Eight strains (CB)	M	Unknown	Unknown	Open Field test/Corticosterone	Some significant diff.	(Gentsch *et al* 1981)
Wistar (LB)	F	Different size	Unknown	Open Field test	Significant diff.	(Gentsch *et al* 1982)
Wistar (CB)	M	Unknown	Unknown	Corticosterone	Significant diff.	(Greco *et al* 1989)
Lister Hooded (CB)	M	Different size	Grid	Open Field test	Significant diff.	(Hall *et al* 1997a)
Lister Hooded (CB)	M	Different size	Grid	Object Contact test	Significant diff.	(Hall *et al* 1997b)
SHR (LB)	M	Different size	Unknown	Blood circulation	Non-significant diff.	(Hallback 1975)
Wistar (LB)	M/F	Different size	Grid	Biochemistry	Significant diff.	(Hatch *et al* 1965)
Wistar (LB)	M	Different size	Grid/Bedding	Open Field test/Biochemistry	Significant diff.	(Heidbreder *et al* 2000)
Sprague Dawley (LB)	F	Same size	Bedding	Open Field test	Significant diff.	(Holson *et al* 1988)
Sprague Dawley (LB)	F	Different size	Grif/Bedding	Open Field test/Corticosterone	Non-significant diff.	(Holson *et al* 1991)
Wistar (LB)	M	Same size	Grid	Corticosterone/Behaviour	Significant diff.	(Holson *et al* 1997)
Wistar (LB)	F	Same size	Grid	Corticosterone/Behaviour	Significant diff.	(Holson *et al* 1991)
Wistar (??)	M	Unknown	Unknown	Pharmacy	Significant diff.	(Kostowski *et al* 1977)
Wister (CB)	M	Differnet size	Unknown	Open Field test	Non-significant diff.	(Niesink & van Ree 1982)
Sprague Dawley (CB)	M	Same size	Unknown	Growth	Significant diff.	(O'Connor & Eikelboom 2000)
Wistar (??)	F	Different size	Unknown	Growth/Biochemistry	Significant diff.	(Pérez *et al* 1997)
Lewis (CB)	M	Different size	Unknown	Corticosterone	Significant diff.	(Plaut & Grota 1971)
Unknown	F	Different size	Unknown	Open Field test	Significant diff.	(Sahakian *et al* 1977)
Long Evans (CB)	M	Different size	Grid	Pharmacy	Significant diff.	(Schenk *et al* 1987)
Long Evans (??)	M	Different size	Grid	Pharmacy	Non-significant diff.	(Schenk *et al* 1988)
Sprague Daley (CB)	F	Same size	Bedding	Blood circulation	Some significant diff.	(Sharp *et al* 2003)
Sprague Dawley (CB)	?	Unknown	Unknown	Growth	Non-significant diff.	(Sobel *et al* 1979
Sprague Dawley (LB)	M	Different size	Unknown	Elevated Plus Maize test	Significant diff.	(Stanford *et al* 1988)
Sprague Dawley (CB)	M	Different size	Grid	Corticostone/Growth/Open Field	Some significant diff.	(Stern *et al* 1960)
Wistar (??)	M/F	Different size	Bedding	Mating Skills	Significant diff.	(Swanson & van de Poll 1983)
CFY and Long Evans (??)	M	Same size	Grid	Growth/Blood circulation	Non-significant diff.	(Szenasi *et al* 1988)
Sprague Dawley (??)	M/F	Different size	Unknown	Corticosterone/Behaviour	Non-significant diff.	(Viveros *et al* 1990)

CB= Commercial Breed; LB= Local Breed at the facility; M=Male; F=Female; ??=Unknown.

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Table 2 Results from a literature review on individual housing of mice. Information about strain, sex, cage size and flooring conditions are given.

Strain	Sex	Cage size	Flooring conditions	Parameters	Analysis (Individual vs group)	Article
TO (??)	M	Same size	Unknown	Open Field test	Some significant diff.	(Benton & Brain 1979)
TO (CB)	F	Same size	Unknown	Open Field test/Corticosterone	Some significant diff.	(Benton & Brain 1981)
ICR (CB)	M	Same size	Unknown	Social skills	Significant diff.	(Cairns *et al* 1985)
CD-1 (CB)	M	Same size	Bedding	Social skills	Significant diff.	(de Catanzaro & Gorzalka 1980)
DBA (CB)	M/F	Different size	Unknown	Emergence test/Growth	Non-significant diff.	(Einon *et al* 1981)
Swiss-Webster (??)	M	Different size	Bedding	Open Field test/Pharmacy	Significant diff.	(Faggin & Palermo-Neto 1985)
TO (CB)	M	Same size	Unknown	Open Field test/Corticosterone	Some significant diff.	(Goldsmith *et al* 1978)
Albino Swiss (??)	M	Unknown	Unknown	Pharmacy	Significant diff.	(Kostowski *et al* 1977)
Albino Swiss (??)	M	Unknown	Unknown	Corticosterone/Behaviour	Non-significant diff.	(Misslin *et al* 1982)
C57BL/6J (CB)	M	Same size	Unknown	Growth	Significant diff.	(Nagy *et al* 2002)
DBA/2 (CB)	M	Same size	Unknown	Pharmacy	Significant diff.	(Puglisi-Allegra & Oliverio 1983)
DBA/2 and T1 (CB)	M/F	Different size	Bedding	Elevated Plus Maze test	Non-significant diff.	(Rodgers & Cole 1993)
NMRI (CB)	M	Same size	Bedding	Blood circulation	Significant diff.	(Spani *et al* 2003)
dd-D (??)	M/F	Same proportion	Unknown	Growth	Significant diff.	(Takemoto *et al* 1975)
ICR (CB)	M	Different size	Bedding	Barbiturate sleeping time	Significant diff.	(Watanabe *et al* 1992)
CAW:CRFW (CB)	F	Same size	Bedding	Corticosterone/Growth/Open Field	Significant diff.	(Weltman *et al* 1968)
CF-1 (CB)	M	Different size	Unknown	Pharmacy	Significant diff.	(Wilmot *et al* 1986)

CB= Commercial Breed; M=Male; F=Female; ??=Unknown.

minimised by small procedural and housing changes eg providing enrichment for the animals. Therefore, future research in this area should be directed at discovering such changes, as scientific research currently has a requirement for individual housing of rats and mice. But until we have the results from new research, we should give the animal the benefit of the doubt, and not recommend any changes in the present state of the art, regarding housing of rats and mice, and therefore only use single housing when integral to the research. We should also be aware of the possibility that this single housing may not influence the animals as much as assumed thus far.

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