*Supplementary Materials*

**A systematic review of the effect of stress in animals during adolescence, and its long-term consequences during adulthood: focus on hippocampal neurogenesis, cognitive function and behavioural outcomes**

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**Supplementary Methods:**

*Inclusion and exclusion criteria*

Included studies had to meet the following criteria: *in vivo* studies in either rats or mice, using a biological or behavioural model of stress-related depression within the adolescence timeframe between PND21-PND65, assessing direct or indirect hippocampal neurogenesis *and* hippocampal-dependent cognitive or depressive-like behavioural outcome in the same period. Keywords for direct measures of neurogenesis included *proliferation*, *differentiation*, or *cell survival*, while indirect measures were searched with *long-term potentiation*, *long-term depression*, *hippocampal volume*, or *synaptogenesis*. In line with the literature, selected hippocampal-dependent cognitive functions included memory, recognition, or pattern separation abilities, while depressive-like behaviour was assessed measuring behavioural despair or anhedonia.

Studies were excluded if they met the following criteria: not in the English language, clinical studies, or in vivo studies not using rats or mice, studies modelling other psychiatric disorders such as schizophrenia, autism, or substance abuse, studies modelling neurological or neurodegenerative conditions, including epilepsy, ischemic stroke, neuropathic pain, Alzheimer’s disease, Parkinson’s disease.

*Search algorithm used*

(((((neurogenesis[Title/Abstract]) OR (progenitor[Title/Abstract]) OR (neuron\*[Title/Abstract]) OR (cell survival[Title/Abstract]) OR (cell proliferation[Title/Abstract]) OR (volume[Title/Abstract]) OR (synap\*[Title/Abstract]) OR (long-term potentiation[Title/Abstract]) OR (long-term depression[Title/Abstract])) AND ((hippocamp\*[Title/Abstract]) OR (dentate gyrus[Title/Abstract]) OR (DG[Title/Abstract]))) OR (((learning[Title/Abstract]) OR (recognition[Title/Abstract]) OR (avoidance[Title/Abstract]) OR (freezing[Title/Abstract]) OR (memory[Title/Abstract]) OR (attention[Title/Abstract]) OR (pattern separation[Title/Abstract]) OR (depression-like[Title/Abstract]) OR (depressive-like[Title/Abstract]) OR (anhedon\*[Title/Abstract]) OR (despair[Title/Abstract]) OR (forced swim test [Title/Abstract]) OR (sucrose preference[Title/Abstract]) OR ((model[Title/Abstract]) AND (depress\*[Title/Abstract]))) AND ((hippocampus-dependent[Title/Abstract]) OR (hippocamp\*[Title/Abstract])))) AND ((((interferon alpha) OR (IFN) OR (cytokin\*) OR (inflamm\*) OR (LPS) OR (cortisol)) AND (depress\*)) OR ((model[Title/Abstract]) AND (depress\*[Title/Abstract])) OR ((((chronic) OR (acute) OR (restraint) OR (social)) AND (stress)) OR (isolation)))) AND (((rat) OR (mice) OR (mouse) OR (in vivo) OR (rodent)) AND ((juvenile) OR (adolescen\*) OR (puberty) OR (age-dependent)))

*Search process*

Studies were extracted from the electronic databases (PubMed, Embase, Psycinfo, Web of Science) by two of the authors independently (J.G. and G.M.). The results were then compared to ensure reproducibility and accuracy of the algorithm. Subsequently, the extracted studies were filtered for screening and selection by each of the authors, and discussion was carried out in case of disagreement.

*Figure credits*

Figures were created with BioRender.com

**Figure:**

Full-text articles excluded, with reasons
(n = 333)

-Clinical studies, *in vitro,* or *in vivo* studies not using rats or mice

-Studies modelling other psychiatric, neurological, and neurodegenerative conditions.

-Outcomes were measured in late adulthood

-Pre-natal stress model

-Only behavioural outcome was assessed

Records excluded
(n = 535)

Records screened
(n = 905)

Records after duplicates removed
(n = 905)

## Identification

Records identified through database searching

(n = 1483)

## Eligibility

## Screening

Full-text articles assessed for eligibility
(n = 370)

Studies included in qualitative synthesis
(n = 37)

## Included

**Supplementary Figure 1.** PRISMA flowchart of search results at each step of the systematic review.

**Supplementary Table 1.** SYRCLE risk of bias assessment of selected studies.

| **Study** | **Sequence generation** | **Baseline characteristics** | **Allocation concealment** | **Random housing** | **Blinding****(Performance)** | **Random outcome assessment** | **Blinding****(Detection)** | **Incomplete outcome data** | **Selective outcome reporting** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Ago et al., 2014  | + | - | ? | + | - | - | - | - | - |
|  Buwalda et al., 2013  | - | - | + | + | + | + | + | ? | ? |
| Coppens et al., 2011  | + | + | + | + | + | + | + | + | - |
| Coutellier et al., 2015 | + | - | NA | + | - | + | - | - | - |
| Dayi et al., 2015 | + | - | + | + | + | + | + | + | - |
| Eiland et al., 2012 | - | - | + | + | + | + | - | - | - |
| Gorbunova et al., 2017 | - | - | - | + | - | - | - | ? | + |
| Gröger et al., 2016 | + | - | + | + | - | + | - | + | + |
| Han et al., 2019 | - | + | + | + | + | - | - | - | - |
| Huang et al., 2012 | + | - | + | + | - | + | + | - | - |
| Huang et al., 2021 | - | + | + | + | + | + | + | + | + |
| Ibi et al., 2008 | - | + | + | + | - | - | - | ? | + |
| Iñiguez et al., 2016 | + | + | + | + | + | + | - | - | - |
| Isgor et al., 2004 | - | + | + | + | + | - | + | + | ? |
| Kovalenko et al., 2014 | + | + | + | + | + | - | + | - | + |
| Lanshakov et al., 2021 | + | - | + | + | + | - | + | ? | - |
| Leussis et al., 2008 | - | + | + | + | + | - | - | - | - |
| Leussis and Andersen, 2008 | - | + | + | + | + | + | - | - | - |
| Li et al., 2017 | - | + | + | + | + | + | + | - | - |
| Li et al., 2019 | - | + | + | + | + | + | + | - | - |
| H.-B. Li et al., 2008 | + | - | + | + | + | + | + | - | - |
| Liu et al., 2015 | + | - | + | + | + | + | + | - | - |
| Maggio et al., 2011 | + | - | + | + | + | + | + | + | - |
| McCormick et al., 2012 | - | + | + | - | - | - | - | - | - |
| McCormick et al., 2010 | - | + | + | + | - | + | - | ? | + |
| Mouri et al., 2018 | + | + | + | + | + | + | + | - | + |
| Nickle et al., 2020 | - | + | + | + | + | + | + | - | ? |
| Oztan et al., 2011 | + | + | + | + | + | - | + | - | + |
| Pawley et al., 2020 | + | + | + | + | + | - | + | ? | - |
| Pinzón-Parra et al., 2019 | + | + | ? | ? | + | - |  - | - | - |
| Pisu et al., 2016 | + | - | + | + | + | + | + | + | + |
| Provensi et al., 2019  | - | - | + | + | + | + | + | + | - |
| Sun et al., 2020 | + | + | + | + | + | + | + | - | + |
| Tsoory et al., 2008 | - | - | + | + | + | - | + | + | - |
| Tsoory et al., 2010 | - | - | + | + | + | - | + | + | - |
| Tzanoulinou et al., 2020 | - | - | + | + | + | + | + | - | - |
| Uysal et al., 2012 | + | + | + | + | + | - | + | + | ? |

(+) high risk, (-) low risk, (?) unknown, (NA) Not Applicable