Max Planck Institute of Psychiatry

IMPRS From Biology to Medicine

The mismatch hypothesis: A new way of linking early experiences and adult environment to vulnerability to stress

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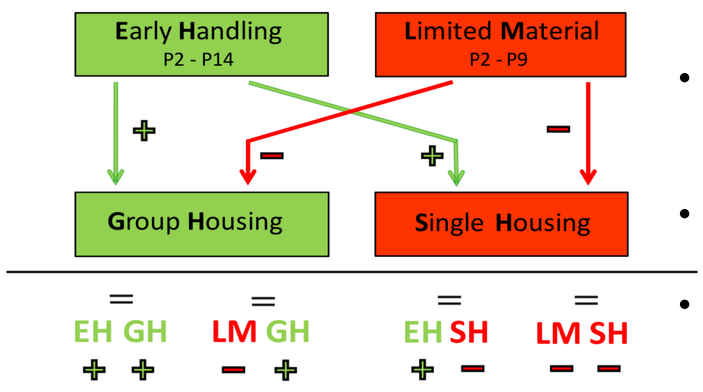
Background

- Chronic stress is one of the main risk factors for depression. Interestingly, not all individuals develop psychopathology after chronic stress.
- **Mismatch hypothesis** proposes that individuals experiencing high levels of psychosocial stress early in life are programmed for dealing with high psychosocial stress and are therefore resilient to high stress levels in later life.

Aim

Is vulnerability to stress increased when there is a mismatch between early and adult environment?

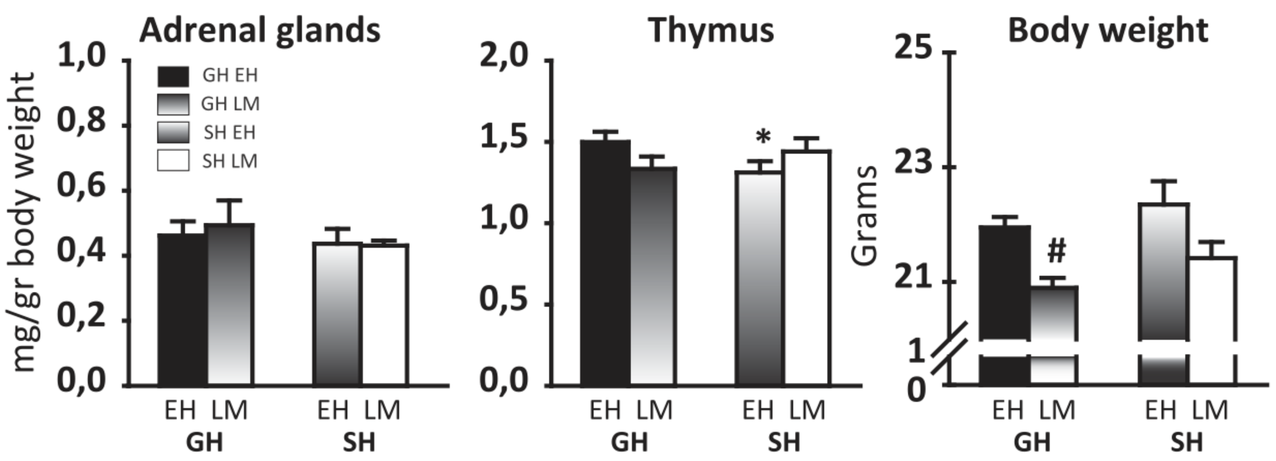
Experimental design



- Animals: female Balb/c mice
- Early life: pups raised with limited nesting material or early handled
- Adult life: single or group housing
- Behavioural test: elevated plus maze, open field, sociability, forced swim stress

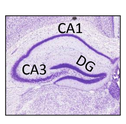
Results

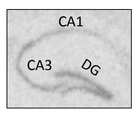
Physiology



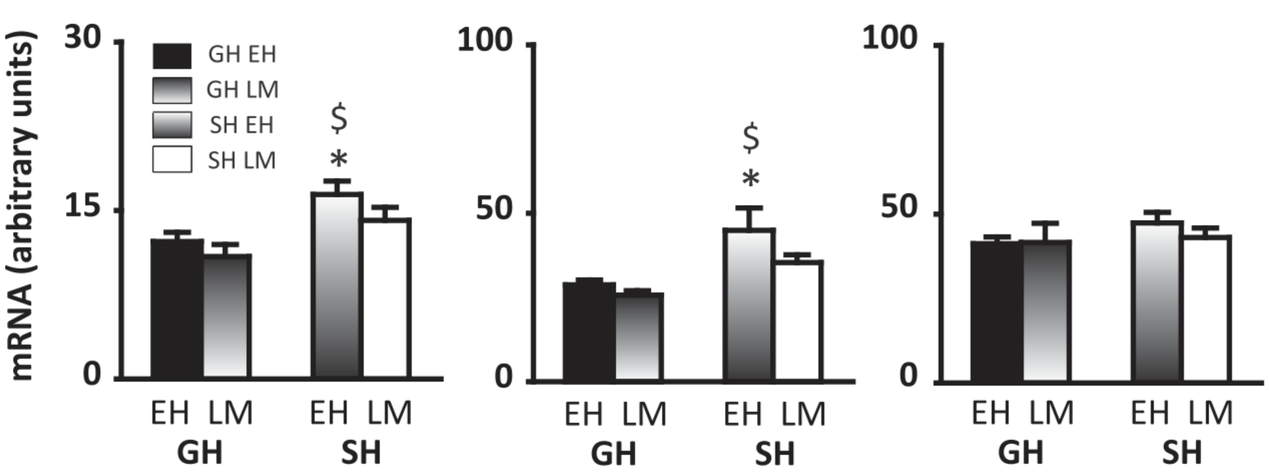
Mismatched animals have **smaller** thymus size

Gene expression profile in dorsal hippocampus



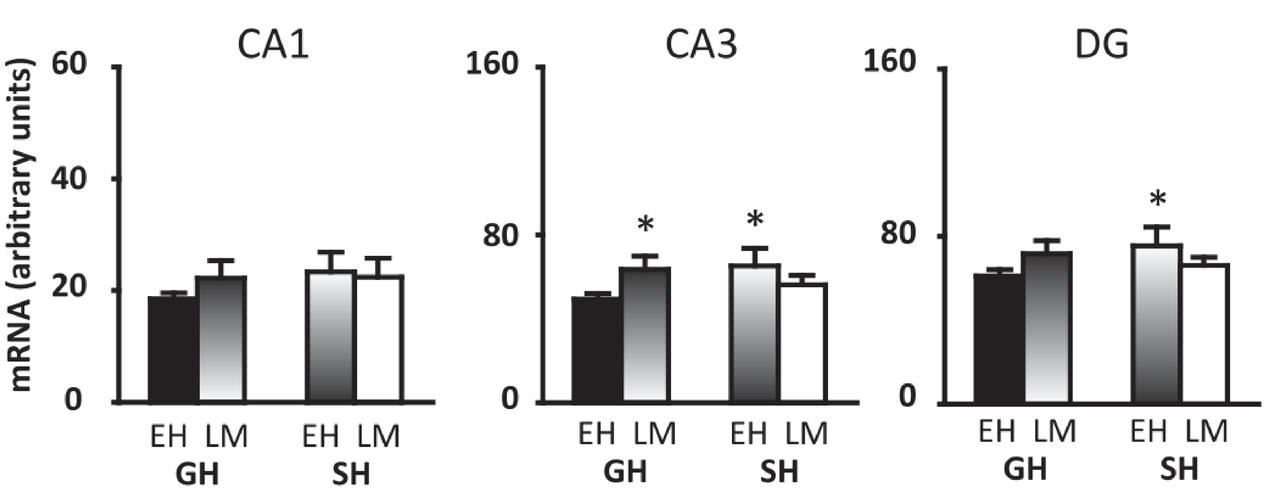


BDNF



BDNF mRNA levels are **increased** in CA1 and CA3 in mismatched animals

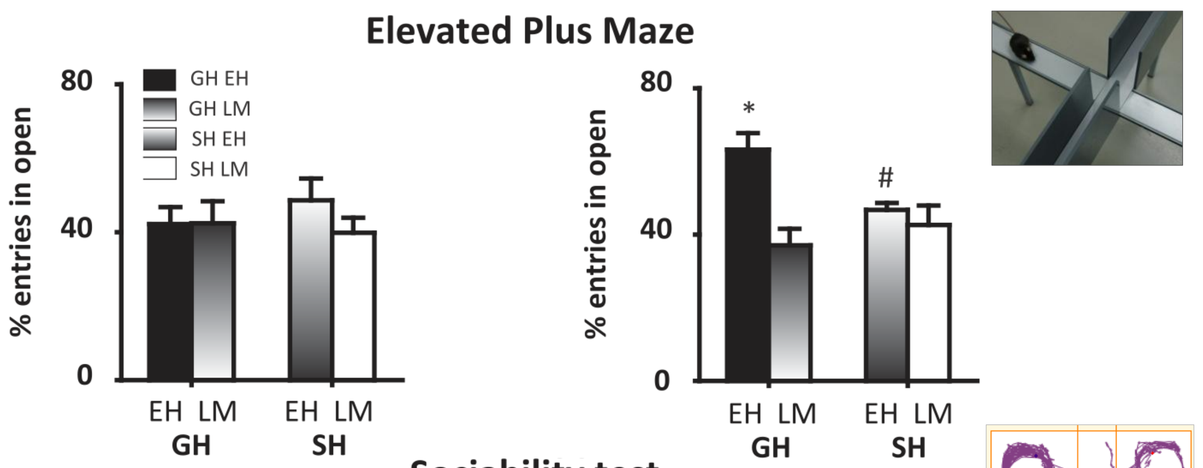
SLC6A15

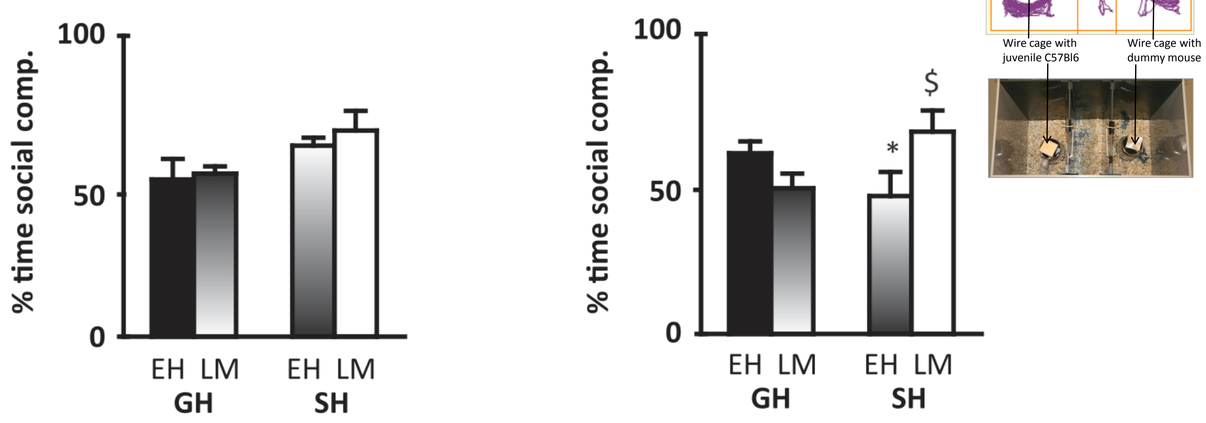


SLC6A15 mRNA is **increased** in CA3 and DG in mismatched animals

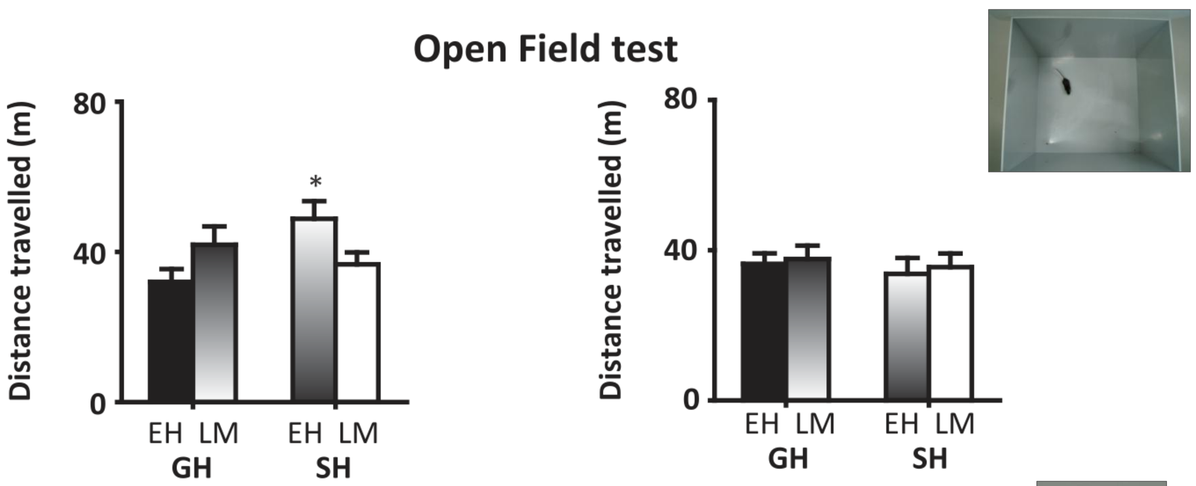
Statistics: *=interaction effect; #= early life effect; $= adult life effect

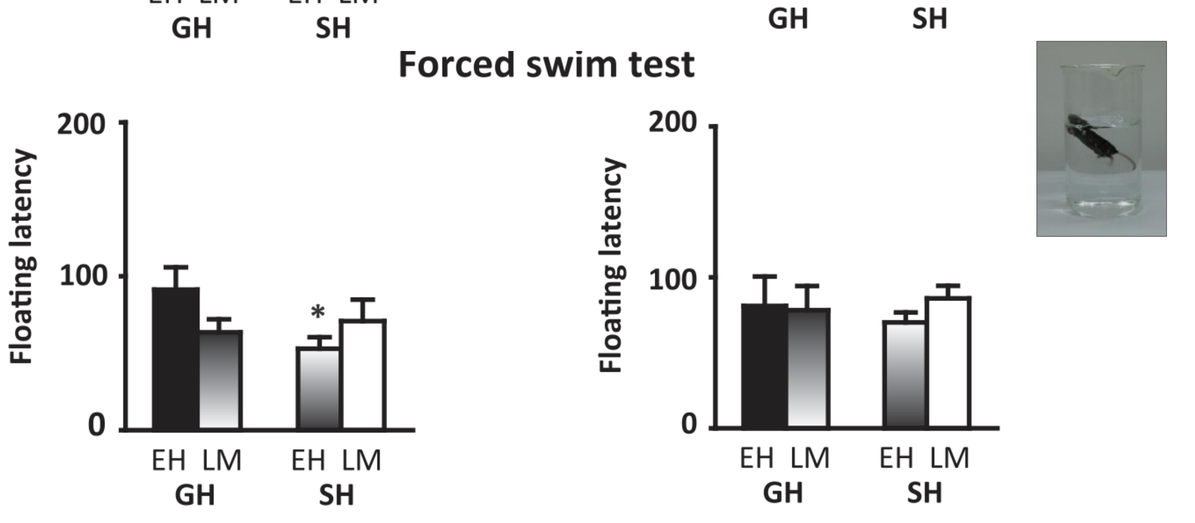
Behaviour





In estrous phase, matched animals are **less anxious** and **more prone** to social interaction, compared to mismatched





In non estrous phase, mismatched animals show **higher locomotion** and **lower latency** to show despair behaviour, compared to mismatched

Conclusion

- Mismatched animals have lighter thymus
- mRNA levels of BDNF and of SLC6A15 are increased in the dorsal hippocampus of mismatched animals
- During estrous, mismatched animals showed less anxiety-like behaviour and lower sociability levels
- In non estrous, mismatched animals showed higher locomotion and higher depressive like behaviour

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