

# Is less prednisolone better?

Low concentrations of prednisolone acetate (PA) are beneficial in mouse slow twitch muscle fibre bundles

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## Aims

1. To investigate the acute, non-genomic effects of prednisolone acetate (PA) on skeletal muscle contraction
2. To investigate the cellular signalling events mediating these actions

## Why do the research?

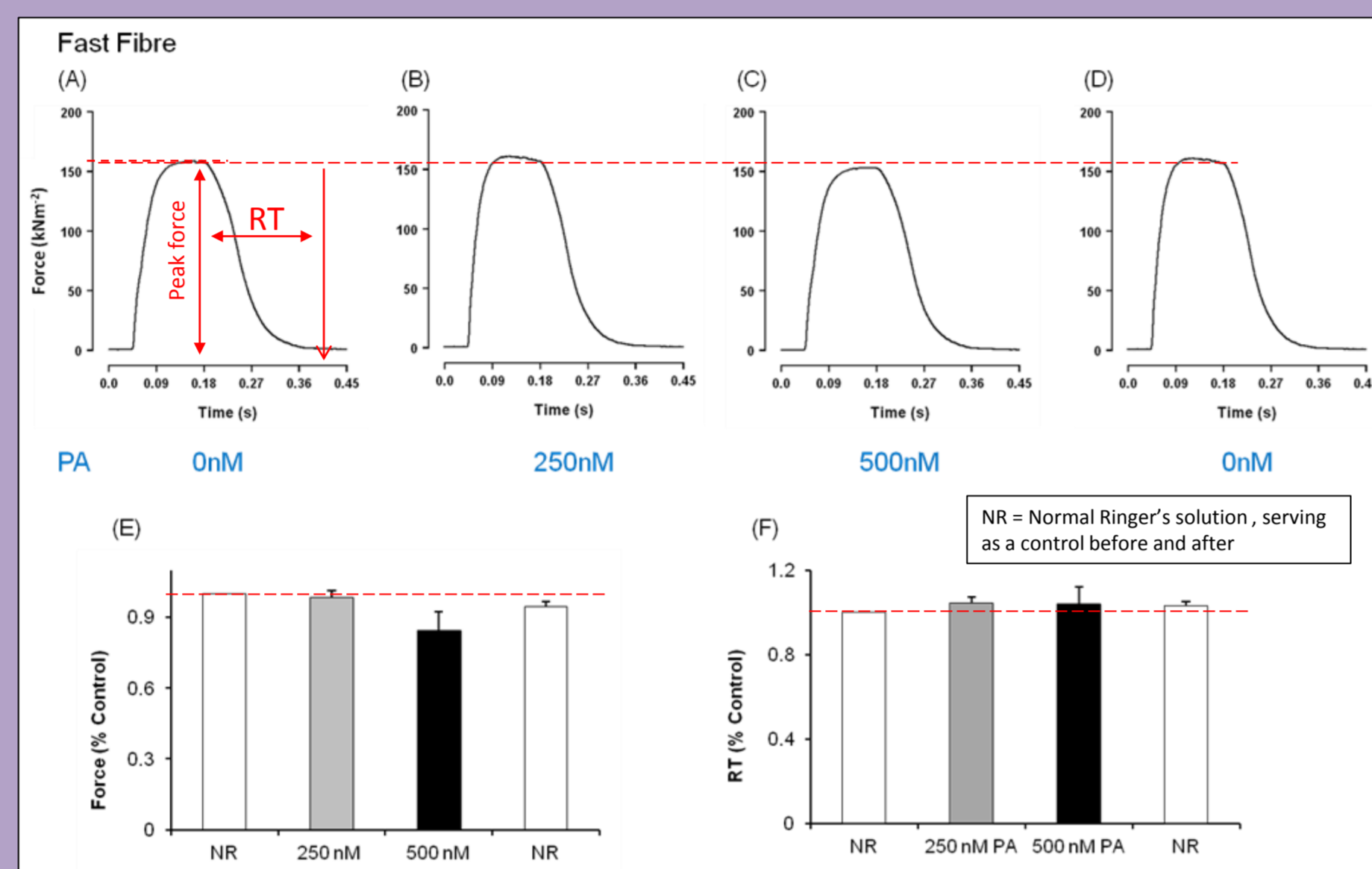
- Glucocorticoids (GCs) are used for managing pain and inflammation.
- When given for long periods and at high concentrations they can lead to muscle wasting
- The muscle wasting is due to their genomic actions
- However, GCs also have acute, non-genomic effects
- These may contribute to the anti-inflammatory properties
- We looked at these in PA, a GC

## Importance

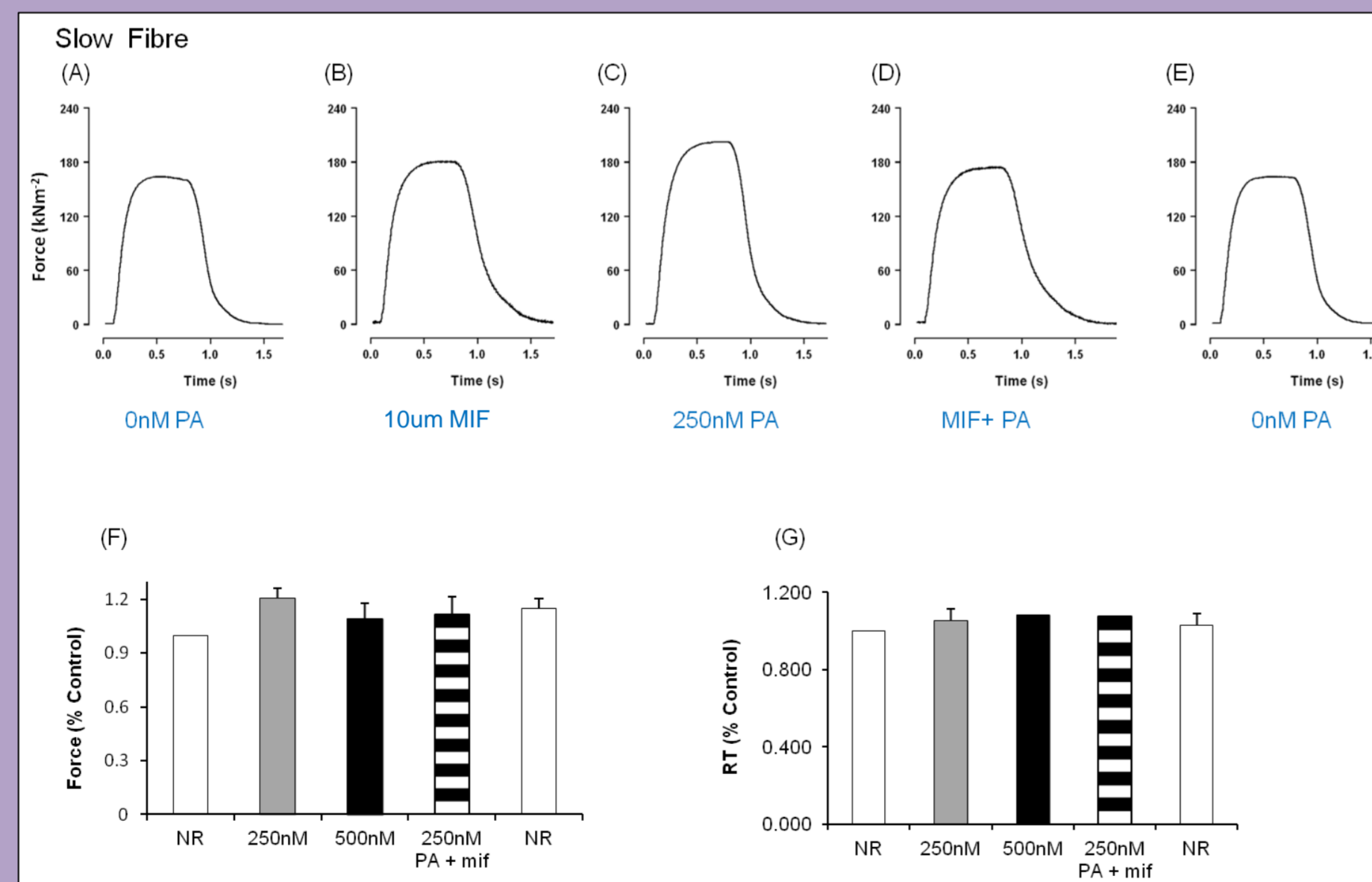
Understanding the acute mechanism may help in the development of drugs which provide the benefits of GCs without the side effects. Modifying therapy may allow some patients live longer and better lives

Abbreviations: PA = prednisolone acetate; GC = glucocorticoid; ERK = extracellular signal-regulated kinase; JNK = c-Jun N-terminal kinases

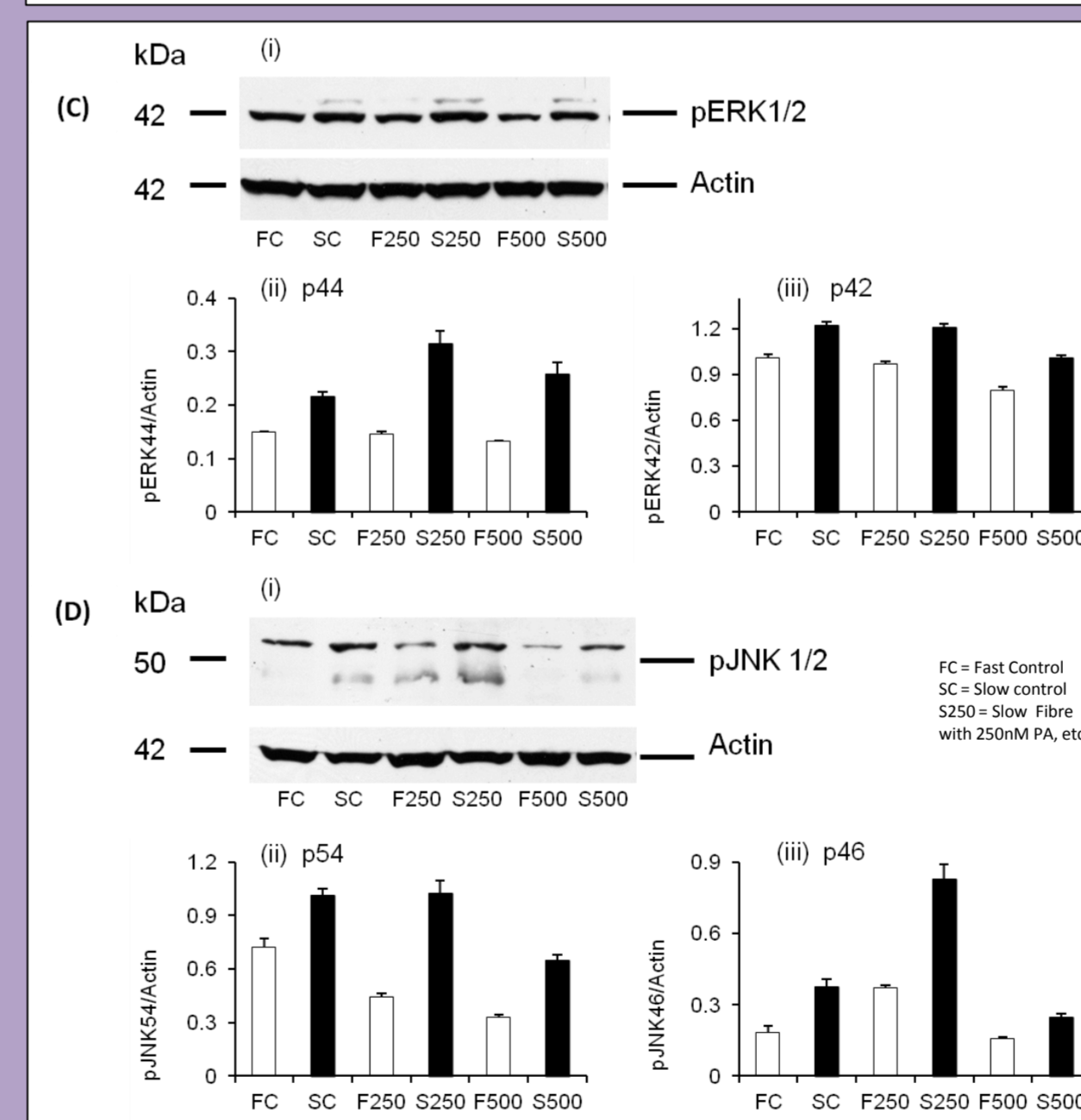
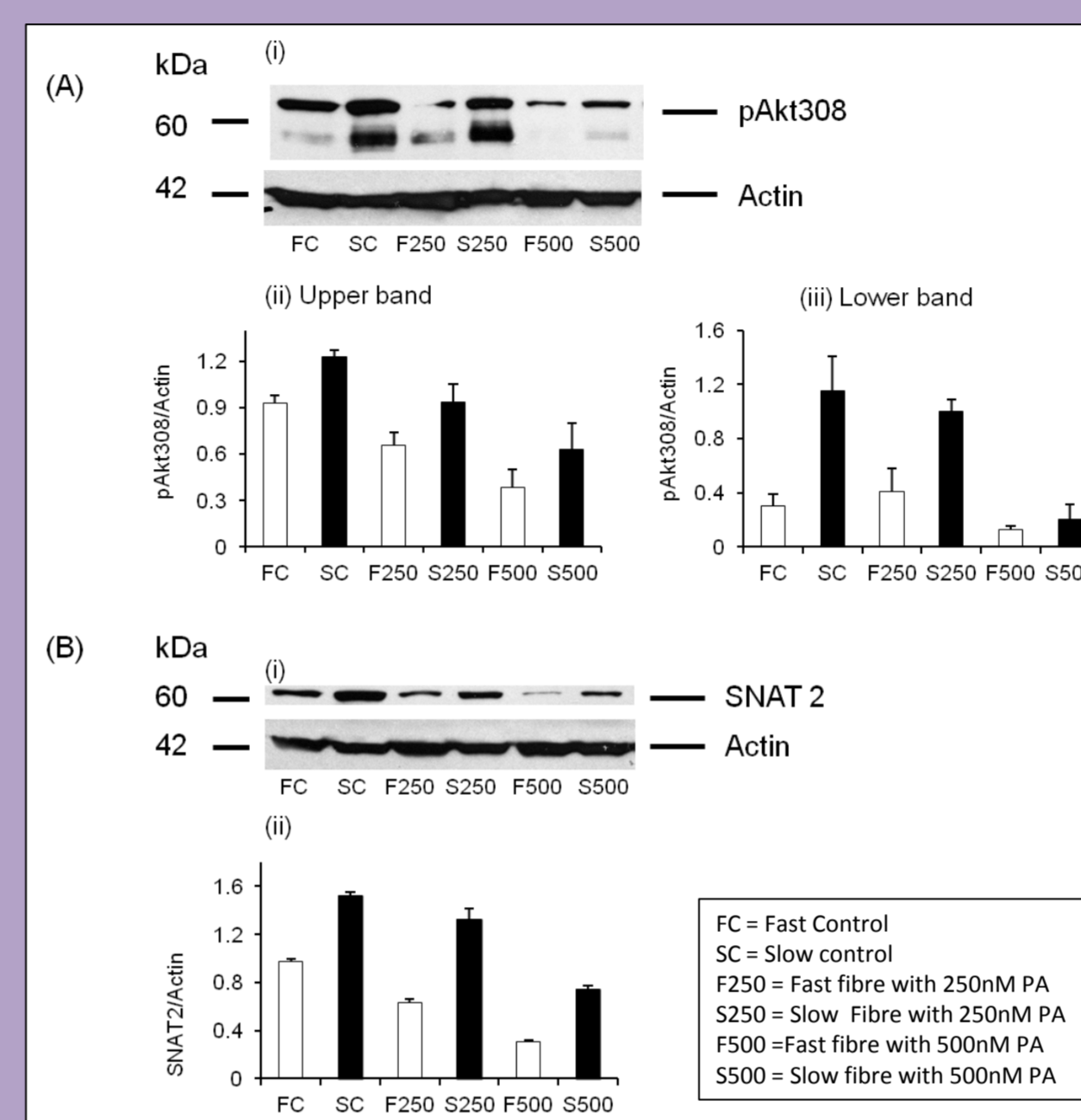
## What did we find?



(1) All concentrations of PA had no effect on force or relaxation time (RT) in fast muscle fibres



- (2) Low concentrations of PA increased force produced in slow muscle fibres
- (3) All concentrations of PA had no effect on relaxation time in slow muscle fibres
- (4) The increase in force was reversed by mifepristone, the glucocorticoid receptor (GCR) inhibitor



- (5) Low doses of PA did not affect the concentration or the activity of the proteins that control protein synthesis (A), amino acid transport (B) and muscle type (C and D).
- (6) However, high doses of PA decreased both the concentration and activity of the proteins.

## Methods

- Fast and slow muscle fibres taken from mice.
- Fibres were exposed to 250nM or 500nM prednisolone acetate added to mammalian Ringer's solution.
- Muscles were electrically stimulated and the contractions were recorded.
- To investigate whether the GC receptor was involved, the GC receptor inhibitor mifepristone was used in some experiments.
- Labelled antibodies were used to investigate the effects of PA on the concentration and activation of AKT308, SNAT2, ERK1/2 and p38

## Summary

- The effects of PA in skeletal muscles are dependent on the concentration and the muscle type
- For example, low concentrations of PA increase force/strength in slow muscle fibres only
- These concentrations do not affect protein synthesis, amino acid transport of muscle fibre type like high, chronic doses do
- Slow muscle fibres are the fibres lost in chronic inflammatory conditions

## Conclusion

- Therefore, we think that low concentrations of PA, given for short periods, could benefit patients suffering from these conditions

## Acknowledgements

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