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on their work

Team and advisors



James Harwood

Ex-Neuroscientist, Fellow
of the EQUATOR Network



Chris Westcott

Senior developer, 15 years
experience



Caroline Struthers

EQUATOR Network,
Education and Training
manager



Jennifer de Beyer

Center for Statistics in
Medicine, University of
Oxford

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For a list of types of articles that Addiction publishes, with definitions, further instructions and word limits, see Section 11 below.

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To submit an article to Addiction please read our requirements and ethical principles below and submit your paper using our [online system](#). We aim to get a response to authors within 12 weeks.

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2 → What kind of article is this?

☐ Key A Research

☐ B Systematic review

☐ C Other

Heterogeneous properties of central lateral and parafascicular thalamic synapses in the mouse striatum

T. Allender, J. Harwood*, P. Kossilo*, P. Bolam
* contributed equally.

Anatomical Neuropharmacology Unit

Keywords: thalamus, striatum, intralaminar, parafascicular, central lateral

Abbreviated title: Properties of thalamic afferents of MSNs

Corresponding author:

T. Allender
Anatomical Neuropharmacology Unit

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Keywords: thalamus, striatum, intralaminar, parafascicular, central lateral

Abbreviated title: Properties of thalamic afferents of MSNs

Corresponding author:

T. Allender

Anatomical Neuropharmacology Unit

t.allender@dpag.ox.ac.uk

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Conflicts of Interests

The authors report no conflicts of interests.

Data Access

All data is published and accessible (Irino & Tada 2009)

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Abstract

To understand the principles of operation of the striatum it is critical to elucidate the properties of the main excitatory inputs from cortex and thalamus, and their ability to activate the principal neurons of the striatum, the medium spiny neurons (MSNs). The thalamostriatal projection is heterogeneous and we aimed to study these afferent inputs to MSNs using small localized injections of adeno associated virus carrying fusion genes for channelrhodopsin-2 and YFP, in either the rostral or caudal portions of the intralaminar thalamic nuclei (i.e. the central lateral or parafascicular nucleus) in mice. This enabled optical activation of specific thalamic afferents combined with whole-cell, patch-clamp recordings of MSNs and simultaneous electrical stimulation of cortical afferents, in adult mice.

We found that the subtypes of thalamostriatal synapses differ in their basic properties, short-term dynamics and expression of ionotropic glutamate receptor subtypes. Our results suggest that central lateral synapses are most efficient in driving MSNs, particularly those of the direct pathway, to depolarization as they exhibit large

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Although the thalamostriatal pathway gives rise to similar numbers of synapses on MSNs as does the corticostriatal pathway (Lacey *et al.*, 2005; Fujiyama *et al.*, 2006; Raju *et al.*, 2006; Moss and Bolam, 2008; Doig *et al.*, 2010), the properties of thalamostriatal synapses have proven difficult to study because of the heterogeneity of the projection and the trajectory of the axons connecting the thalamus and striatum. The latter difficulty can be overcome, to some extent, when studying the projection as a single entity, by careful placement of stimulating electrodes and careful selection of the plane of slicing of the brain (Ding *et al.*, 2008; Smeal *et al.*, 2008). However, electrical stimulation cannot isolate different sub-nuclei of the thalamostriatal system. It is clear that different sub-nuclei have different properties; for instance, it has been shown that thalamostriatal neurons in the CL and Pf nuclei differ in their morphology, firing properties, as well as their striatal targets (Lacey *et al.*, 2007), presumably underlying different roles in striatal function. Furthermore, behavioral studies, mainly focused on Pf, have suggested thalamic involvement in a variety of processes (Kendall *et al.*, 2005).

The aim of the work described in this paper was to test the hypothesis that synapses formed in the striatum by neurons originating in different sub-nuclei of the intralaminar thalamus have different functional properties. To address this we set out to isolate and differentially activate the thalamostriatal projection originating in either

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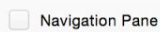
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cortical afferents (mean ratio of S2/S1: 1.00 ± 0.04 , $n = 34$, **Figure 5A**). we did not observe any differences in the PPR of CL, Pf and cortical synapses between direct pathway and indirect pathway MSNs (**Table 1**).

Next, we investigated the dynamics of these inputs during longer trains of stimulation at 5 Hz, 10 Hz and 20 Hz. These analyses revealed a similar picture to that seen during paired-pulse stimulation. The Pf response is significantly depressing following both the 10 and 20 Hz trains and the rate of recovery was the least of all three responses ($t(44) = 3.10$, $p < 0.05$). Whereas all responses depress eventually, only the responses of CL inputs are facilitating for the first few spikes during both 10 and 20 Hz stimulation CL ($t(72) = 1.73$, $p < 0.05$). Secondly, Thus the dynamic properties of CL, Pf and cortical synapses differ in that CL synapses are facilitating whereas Pf and cortical synapses are largely depressing.

We found that this protocol leads to long-term depression of evoked EPSPs at Pf. However, the same protocol applied to CL synapses did not lead to any change in the amplitude of evoked EPSPs ($t(27) = 0.41$, $p < 0.05$; **Figure 5A**).

To investigate the mechanisms underlying this plasticity we repeated the pairing protocol for Pf synapses, but this time included either the calcium chelator, EGTA (10 mM), or the NMDA receptor antagonist, MK-801 (1 mM), in the

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Have you included confidence intervals for every p-value?

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This t statistic is consistent with its p-value using a 2 tailed test

Check thisHave you given your p-values as exact numbers? pnl.pe/1TjwhNX**Check this**Have you justified using a 1 tailed t-test? This p-value is not consistent with a 2-tailed t-test. pnl.pe/22dCrm8**Check this**

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What does it check for?

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Sections and statements:

Acknowledgements, Funding, conflicts of interest, corresponding author

Ethics:

Review board named, informed consent

Figures and Tables:

Present or absent, legends

Statistics:

Double check common hypothesis tests, confidence intervals, percentages with absolute numbers

Referencing:

Correct style, all citations referenced and vice versa

Addiction, 1 month in

53

Submissions

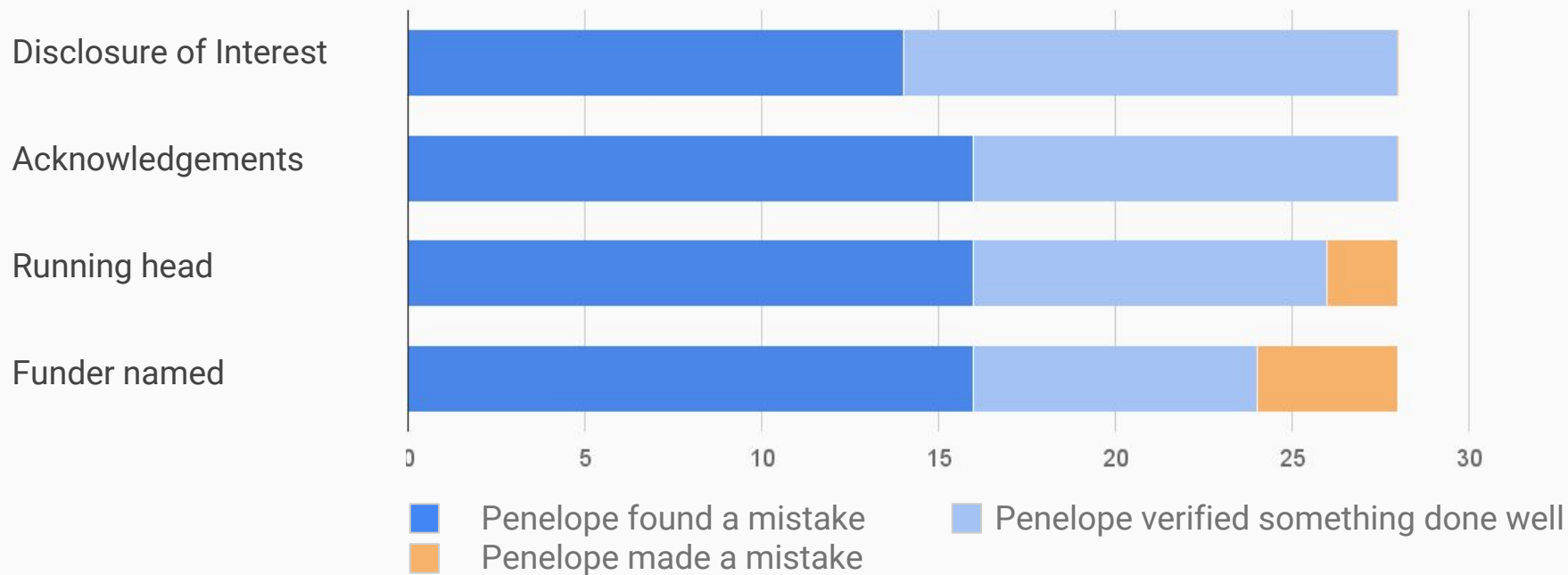
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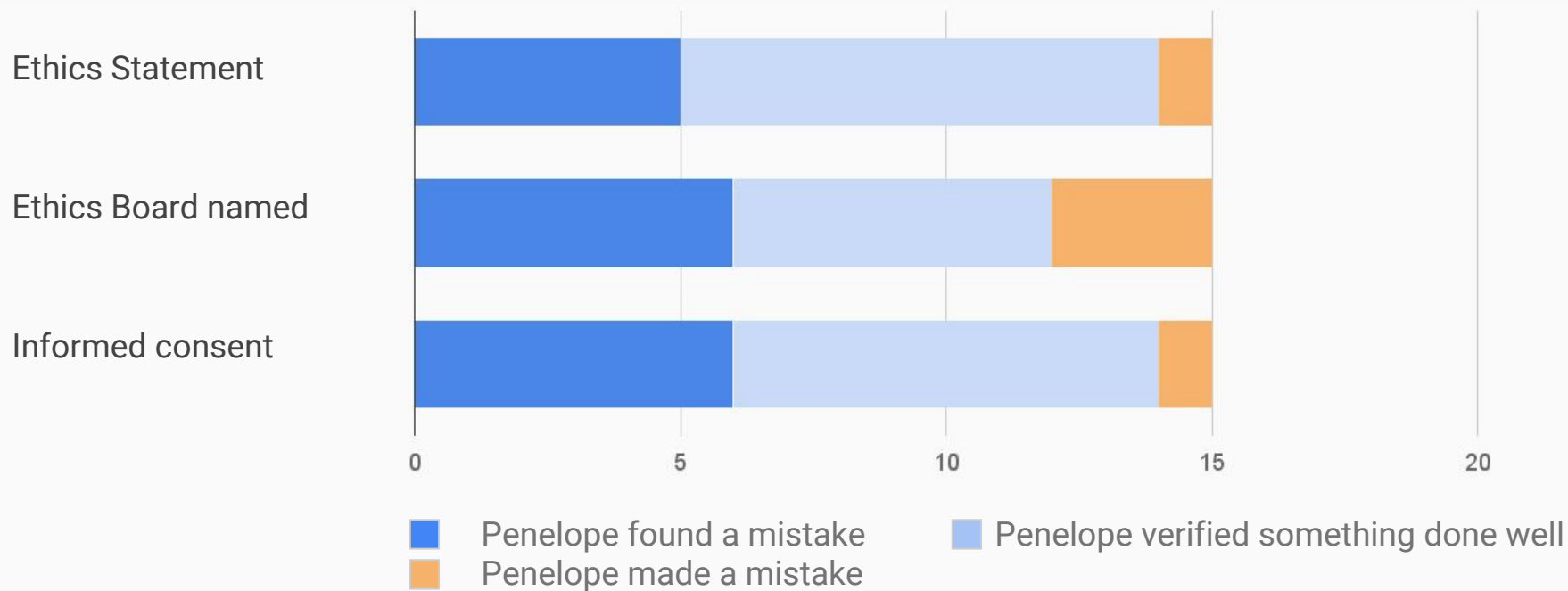
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Suggestions

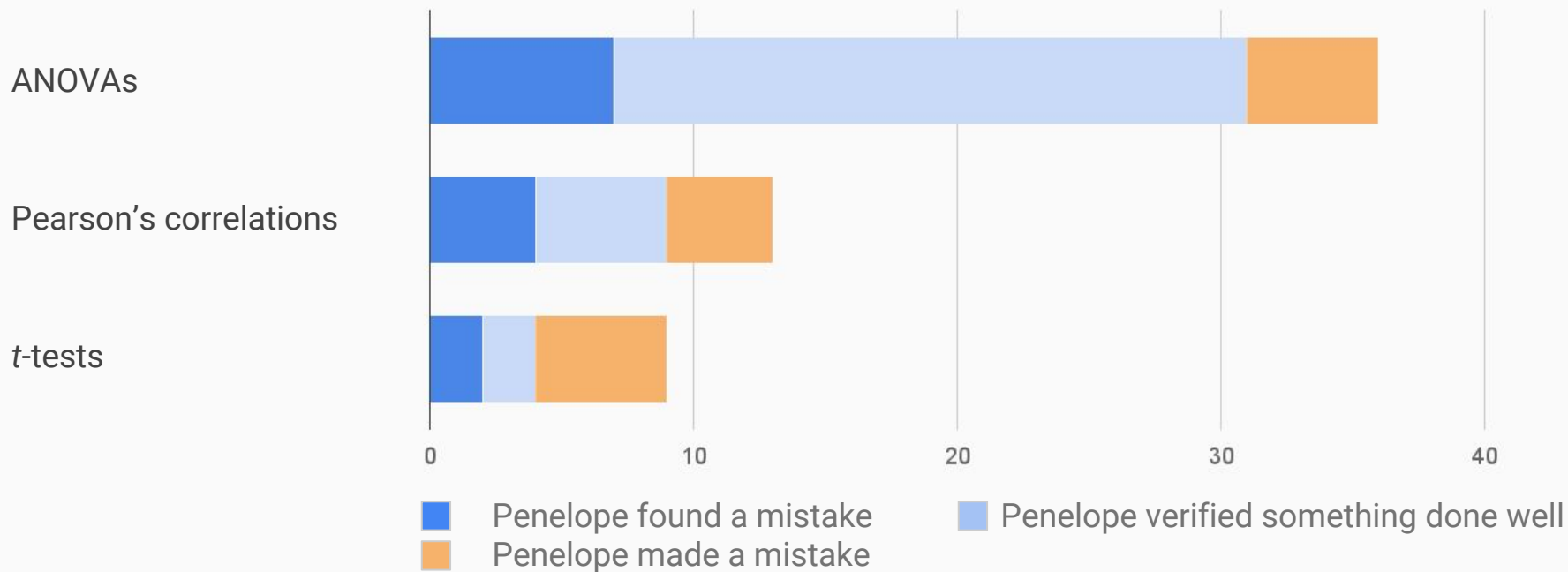
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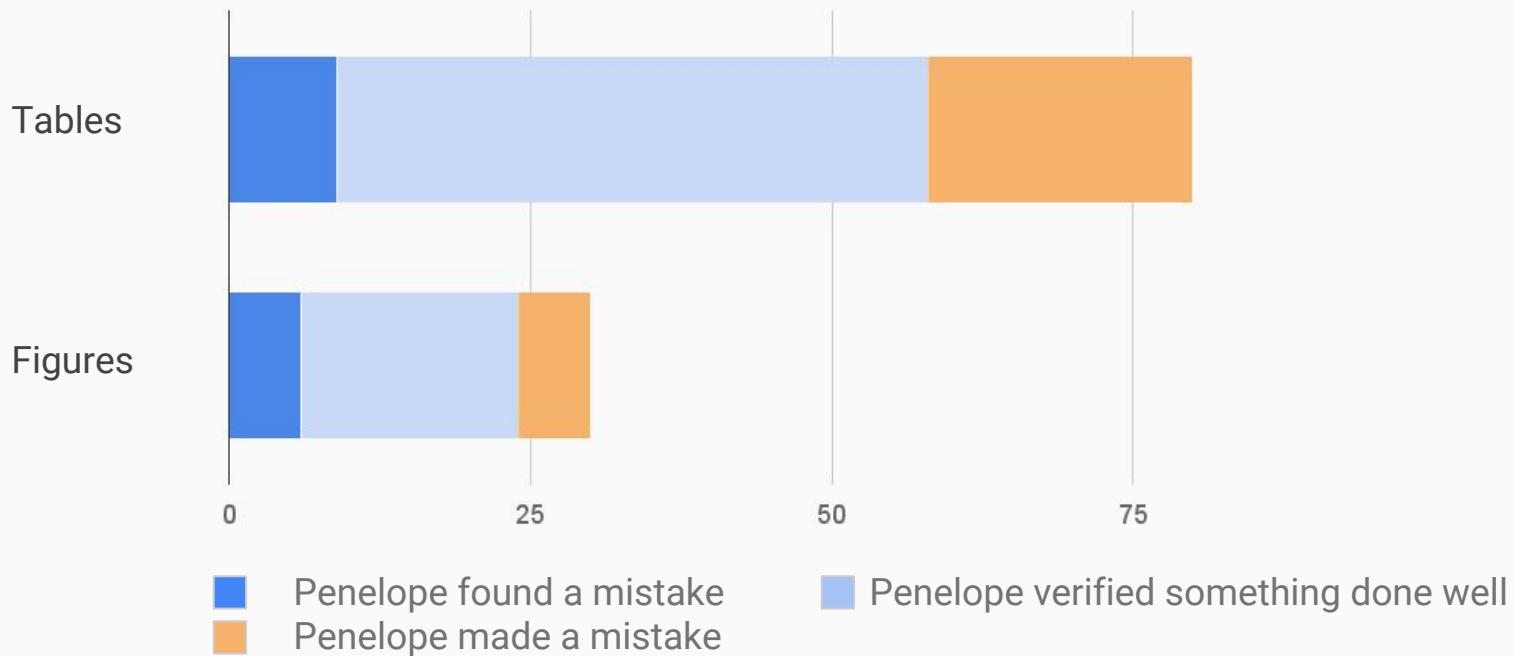
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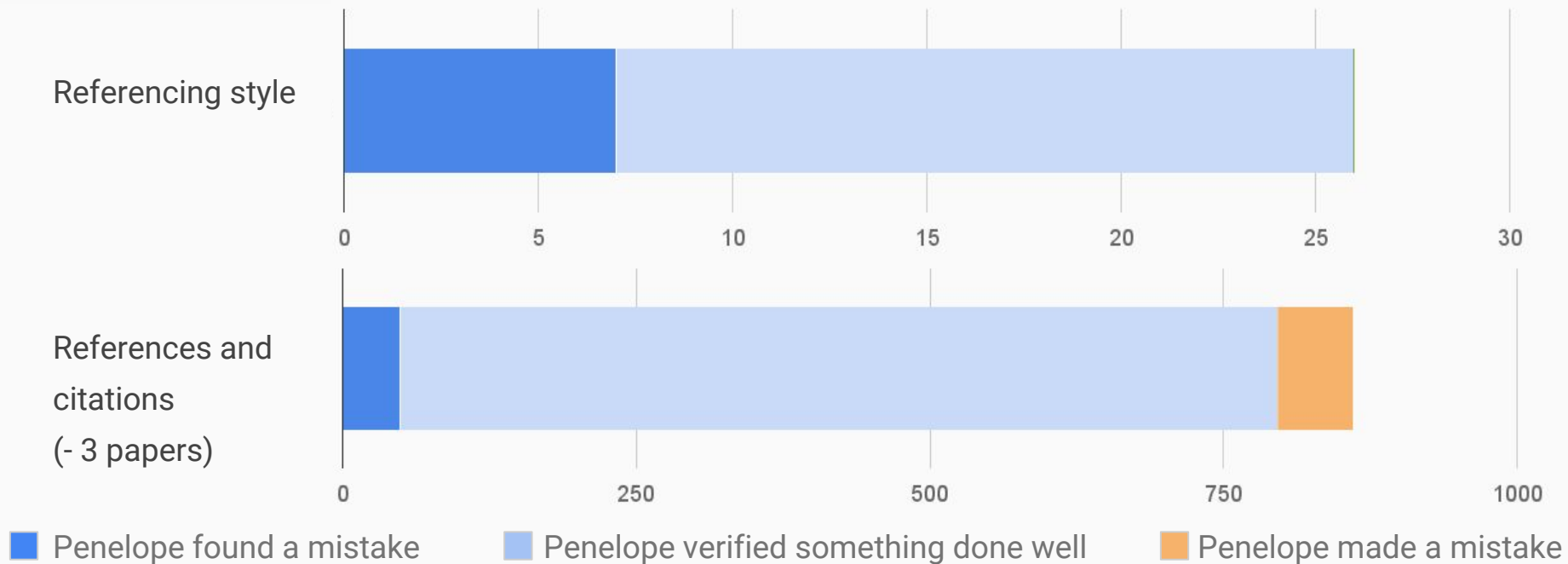
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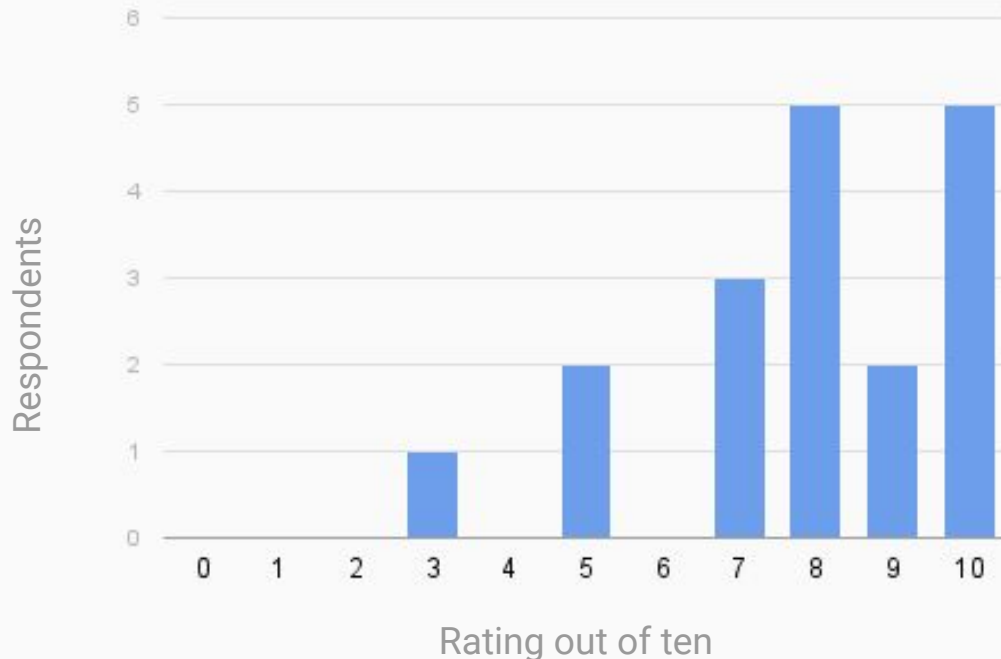


Performance

Other issues:

- There can be too many comments
- Occasionally comments aren't perfectly aligned

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“Very straight forward - extremely quick!” 10/10

“It helped me to become aware of things I had left out.” 10/10

“Helpful comments” 7/10

“It's a great tool and was very helpful; however it wasn't an exact match to my research so more options would be nice.” 7/10

Summary

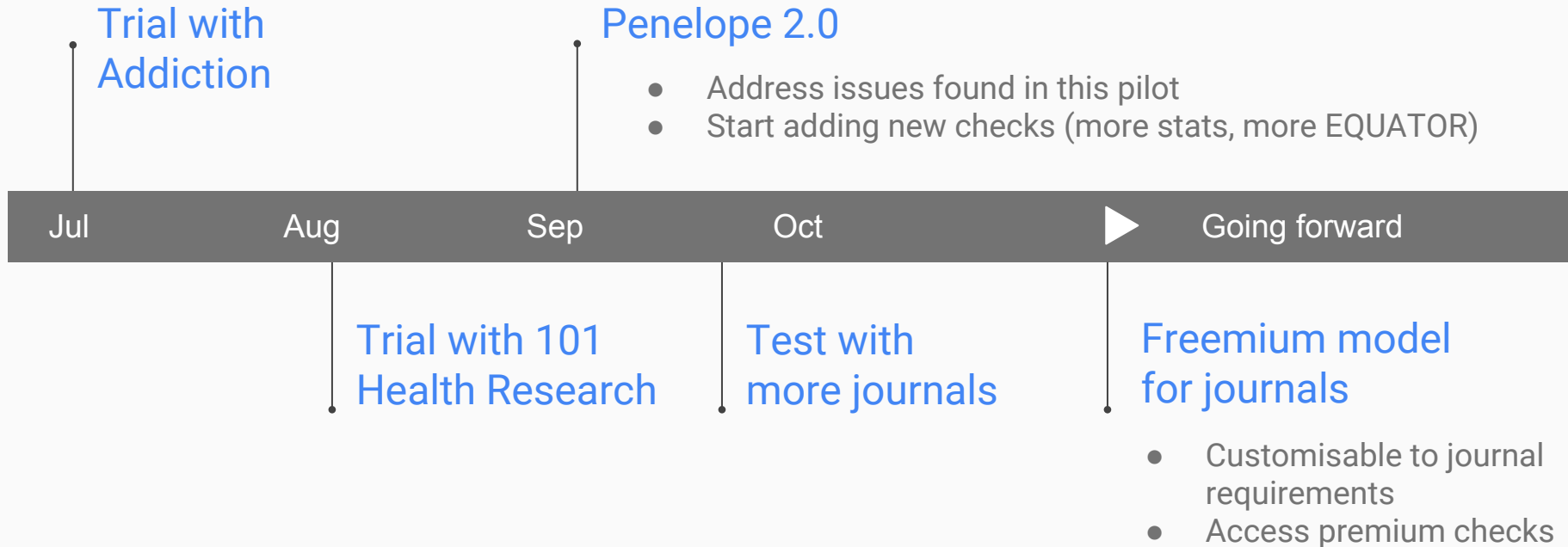
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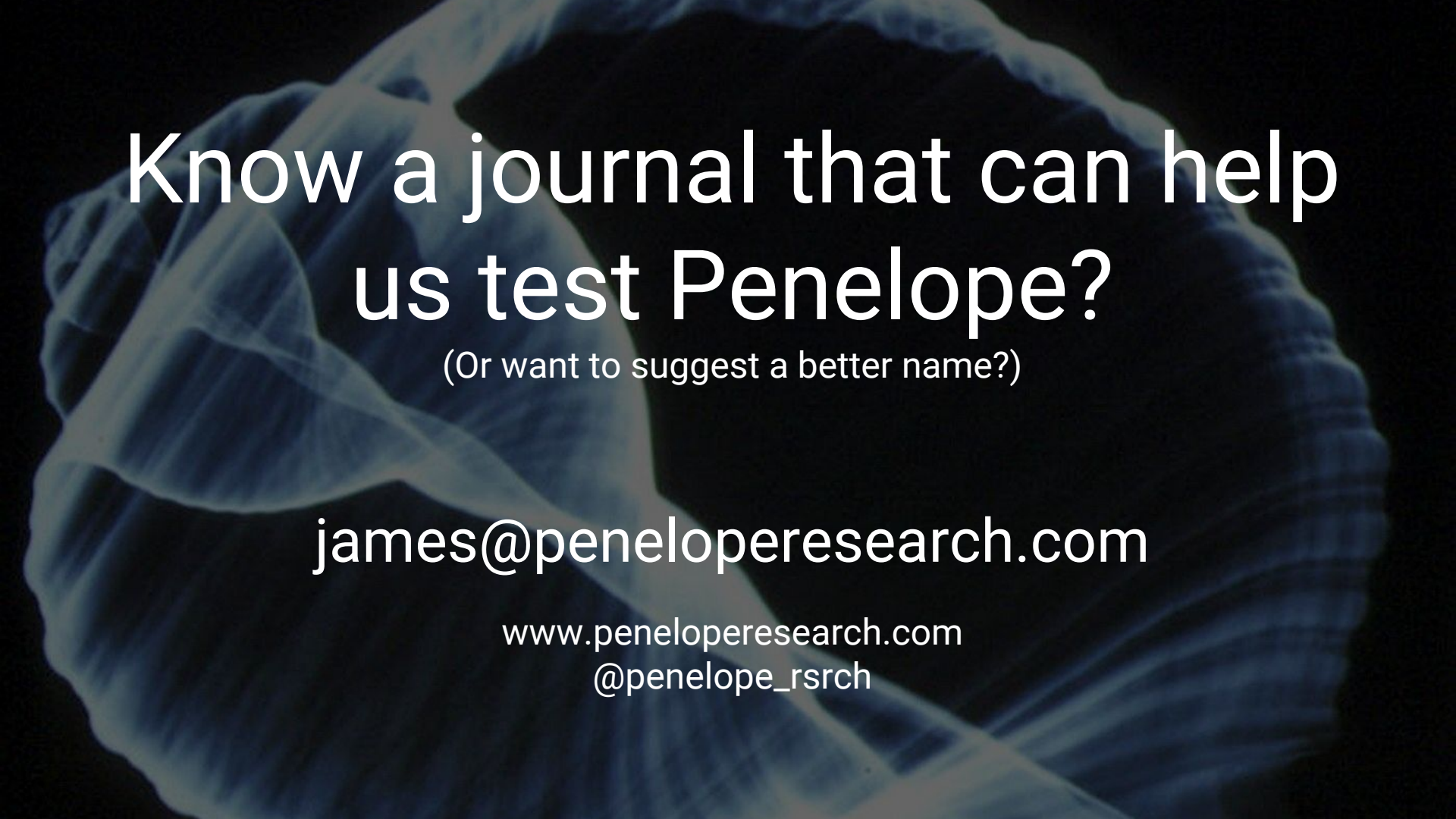
- Authors liked speed and ease
- Many checks perform well
- Successfully caught errors

To be improved:

- Performance of some checks
- Comment overload

Next steps





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