

nAChR. ANI alone evoked minimal responses compared to ACh but suppressed subsequent responses to ACh (Fig 2). ANI produced no detectable responses in oocytes that were not injected with RNA for nAChR subunits (not shown). When 10 μ M of the $\alpha 7$ -selective PAM PNU-120596 [31] was added to the ANI, the $\alpha 7$ -expressing cells showed responses that were much larger than those evoked by ACh alone.

PNU-120596 is known to destabilize desensitized states of $\alpha 7$ nAChR and so typically evokes responses that are much more prolonged than those stimulated by ACh or other $\alpha 7$ agonists [32]. When used in combination with ACh in our system, PNU-120596-potentiated responses normally decay well back to baseline during the normal washout procedure [32]. However, potentiated ANI responses were biphasic and only partially decayed through the washout period. When 60 μ M ACh was applied 4 minutes after the initial ANI application, there was a transient increase in current added to the still decaying responses to the previous application of ANI plus 10 μ M PNU-120596. There are many potentially active molecules in the areca nut, including numerous alkaloids, with the most abundant and active for producing responses in central and peripheral nervous system tissues being arecoline, a muscarinic agonist with activity at M1, M2, and M3-type