**Introduction**

Adolescence is a dynamic phase of brain development associated with a decline in synaptic density, an increase in myelination and a strengthening of neural circuits. This refinement in neural systems is believed to improve the efficiency of the brain and enhance the speed of information flow across neural networks which are critical for optimal decision-making. The neurobiology that mediate these changes in decision making, however, are unknown.

We investigated how decision-making processes, which are controlled by OFC circuits, change across adolescent development in male and female rats.

**Methods**

**Training on the Reversal Learning (RL) task**

Long Evans rats (N=43; 21 F, 22 M) bred in our facility were trained on a three-choice reversal learning (RL) task at either postnatal day (PND) 30 (N=12), 50 (N=12), 70 (N=7) or 90 (N=12). Rats were trained to make operant responses (e.g., nose port entry) to receive an oral delivery of sweetened condensed milk (10% w/v) in 12 h overnight sessions. Rats were then trained to discriminate between three spatial locations using a deterministic schedule of reinforcement. Each time rats reached a performance criterion (e.g., choosing the highest reinforced option 21 times in the last 30 trials) the reward contingencies changed. Sessions terminated when rats received 151 rewards or 12 h had elapsed. After completing 3 overnight sessions on the deterministic RL, decision making was assessed in a probabilistically reinforced RL task. Reward probabilities assigned to each noseport were pseudo-randomly assigned at the start of each session (70%, 30%, and 10%). The reward contingencies changed each time the performance criterion was met. Sessions terminated when rats achieved 151 rewards or 12 h had elapsed. Rats completed 3 overnight sessions on the probabilistic RL and were sacrificed immediately after the last session.

**Reversal learning model**

Trial-by-trial choice data in the RL task was fit with the following reversal learning model which contained four free parameters:

- $a(t)$ and $r(t)$: if $a(t)=+1$ and $r(t)=+1$, $Q(t+1) = r C + \gamma D$; if $a(t)=+1$ and $r(t)=0$, $Q(t+1) = r C + \gamma D$; if $a(t) = -1$, $Q(t+1) = r C + \gamma D$.

- $\gamma_r$: decay rate for chosen options
- $\gamma_u$: decay rate for unchosen options
- $D$: appetitive strength of rewarded outcome
- $A$: aversive strength of no reward outcome

The model was fit separately to the choice data collected in the deterministic and probabilistic RL task and then averaged across the different schedules.

**Adolescence-related changes in signaling pathways**

Brain tissue was collected immediately following the last RL session. Tissue was homogenized and underwent tryptic digestion to generate peptide fragments. Digested peptides were submitted to the Yale-NIDA Neuroproteomics Core where they will be separated on an Ultra high-pressure liquid chromatography (LC) system and analyzed by LC-MS/MS. Peptide precursors were isolated and fragmented to produce a measure of peptide abundance. We will compare protein abundance across adolescent development and examine the relationship between protein expression and decision making.

**Decision making improves across adolescence**

The model was fitted separately to the choice data collected in the probabilistic RL task at each of the postnatal day (PND) 30 (N=12), 50 (N=12), 70 (N=7) or 90 (N=12). The reward contingencies changed at the start of each session (70%, 30%, and 10%). The reward contingencies changed each time the performance criterion was met. Sessions terminated when rats achieved 151 rewards or 12 h had elapsed. Rats completed 3 overnight sessions on the probabilistic RL and were sacrificed immediately after the last session.

**Conclusions**

These data demonstrate that improvements in flexible decision making that occur during adolescence are related to reward-mediated updating. Based on our previous work demonstrating that action value updating following rewards is controlled by the amygdala→OFC circuit, we hypothesize that maturation of the amygdala→OFC circuit may be critical for the age-related improvements in decision making we observed here. Our ongoing proteomic studies seek to identify the signaling pathways that are responsible for these decision-making improvements.

**Future directions**

We have found that individual differences in the $\Delta$ parameter prior to any drug use predict future drug-taking behaviors. We hypothesize, therefore, that development disruptions in the amygdala→OFC circuit enhance addiction-like susceptibility. Our ongoing work is using a viral approach to characterize the amygdala→OFC circuit across development to determine if differences in circuit formation in adolescence predicts drug-taking behaviors in adulthood.

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