The Neural Circuits Underlying Fear and Surprise

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The human brain is fascinating. It controls each of the potential decisions we make every single day. The dense, intermingled circuitries provide a great deal of content for scientists to discover and better understand the brain. No matter the differences between each human, emotions are a constant for everyone - especially surprise and fear. These two emotions are hard-wired from birth in every single person. In this review, we will analyze the circuitries of both surprise and fear, and discuss in detail the brain circuitries that the two emotions share and separately engage. We will also discuss the progress that the scientific community has made in better understanding these emotions, the current research, as well as propose future experiments that build upon the foundations of what is known.

Introduction

The human brain is one of the most versatile parts of the human body. It is also the most complex organ with over 86 billion neurons compacted into an approximately 3 pound mass, and is responsible for our survival and decision making[1]. There is no question as to why so many scientists are so fascinated by the brain. emotions felt in the brain play a large part in controlling our behavior. Out of all the emotions humans can feel , surprise and fear are some of the strongest ones. A person can dictate when they feel happy or sad, but pure surprise and fear can not be controlled at all. The distinction between the circuitries is an interesting one we have yet to fully define.

The story of Phineas Gage is one of great value as it is the first documented cases to indicate the brain had control over emotions. Gage was a railroad worker who was accidentally struck with a rod that penetrated his skull from the lower jaw all the way through the top of his head[2]. He suffered immense trauma to the brain, but fortunately he survived. He experienced an evanescent but drastic personality change for the worse as he became very irreverent because of this freak accident[2]. This documented case was one of the first to indicate that the brain had control over emotions and drew interest from the scientific community to better study the brain and its effect on behavior and emotions. Surprise and fear are very related, as one is often fearful in a surprised situation or surprised in a fearful situation[3]. Yet, there are very distinct features for each emotion. Advancements in technology have finally allowed researchers to better study the brain beginning in the last two decades.

Fear

The ability to feel fear is crucial for humans. It is a gear in the machine - our brain - that drives our survival instincts. Researchers have been steadily building the foundation to our understanding of the emotion. Fear manifests in different versions, from phobias to anxiety. However, there is a common circuitry connecting all these versions which could hold answers to long-sought questions regarding PTSD and other fear related illnesses.

The fear circuitry was found to involve the amygdala early on and in 1997, Adolphs et al set out to investigate which parts of the amygdala were crucial to the fear circuitry. They studied three sets of participants - ones with bilateral amygdala damage, ones with unilateral amygdala damage, and ones with no damage to their amygdala. In the study, they had participants recognize a series of faces with and without fearful expressions. They discovered that identifying a face and the recognition of fear are not associated with each other[4].

Bilateral amygdala damage was found to impair judgment of the intensity of faces depicting fear and the ability to detect fear[4]. It could also damage the ability to reconstruct visual images with fear, but it does not affect the concept of fear as the subjects can still verbally describe it[4]. This is because the amygdala connects back to visual cortices, the connections of which are still intact[4]. Unilateral amygdala damage, however, was found to not impair recognizing facial expressions[4]. Overall, bilateral damage hurts the processing of fear in recognition and recall[4]. Ultimately, the study did find that bilateral damage affects the fear circuitry but unilateral damage does not[4].

Eventually, researchers expanded from the amygdala into other brain regions involved in the surprise circuitry. Zhao et al asked participants to differentiate between surprised and

fearful faces. To provide a rigid rubric, they defined a fearful face as one which conveyed a potential threat and frightening event[3]. A fearful face was defined as a raised inner and outer brow, raised upper eyelid, open mouth, brow lower, and the lip stretched[3]. The results of the experiment complemented what Adolphs et al, 1997 found which was that the amygdala plays a huge role in fear circuitry and they even added on by discovering that the amygdala is responsible for monitoring environmental clues[3]. An interesting result of the study was that while the amygdala and parahippocampal gyrus were vital for emotional circuitry, they were of no help distinguishing between fearful and surprised faces[3]. It was also discovered that fear activates more of the memory and attention circuitries than surprise did[3]. In addition, the right hemisphere of the amygdala and the parahippocampal gyrus was active for both fear and surprise[3]. The most important findings of this study, however, was the fact that fear circuitry involves the frontal and temporal lobes, temporal and occipital cortices, and the frontal plus right middle temporal gyrus[3]. To be even more specific: left postcentral gyrus, left middle temporal gyrus, left cuneus, left putamen, left and right inferior occipital gyrus, left and right precentral gyrus, left supplementary motor area, right parahippocampal gyrus, and the right amygdala are all active while recognizing fearful faces[3].

Moving further along in the timeline of fear circuitry exploration, researchers turned their attention to an aspect that hadn't been explored before: size. Tuulari et al, 2020 examined whether variations in the bilateral amygdala volume had an effect on fearful expressions and the attention span. To test this hypothesis, the team studied 8 month old newborns and had them concentrate on a face for a certain amount of time while distractions around them tried to gain their attention. The team tracked their eye movements and compared the results. The results showed that infants were more likely to disengage from fearful faces when their left amygdala size was bigger[5]. The right amygdala, however, showed no such signs of correlation and the left amygdala only seemed to have a correlation with fear[5]. Previous studies even suggest that amygdala maturing is a key part of an infant's attention bias and fear processing (Whalen et al., 2001) which was replicated when amygdala volumes positively correlated with infants getting distracted from a fearsome toy (Cismaru et al., 2016). The larger the left amygdala volume, the higher the probability to disengage - specifically - from fearful faces[5]. This shows how the left amygdala is the only significant part for recognizing fearful faces while staying tuned to them. These findings confirm that not only is the amygdala's overall damage important in fear circuitry but the size of the amygdala too.

Hessl et al also investigated the significance of the amygdala's size. This article hypothesized two different factors that could affect the amygdala: the size and disease. They believed that the fear potentiated startle would increase in children with autism spectrum disorder and that there would be a positive correlation between the magnitude of the fear potentiated startle and the volume of the amygdala. The stimuli were puffs of air and sound to startle the subjects, measured by the speed of their reflexes. An important key word this article uses is anxiety, which is a vital part of the fear circuitry as there cannot be anxiety without fear[7].

These experiments showed that there was an association between the left and right amygdala and the anxiety severity . Even more accurately, for every increase in the left amygdala volume there was an increase in anxiety[8]. This was also mirrored with the right amygdala. This study also found subjects with autism and anxiety had smaller right amygdalas compared to subjects with only autism spectrum disorder[8]. The relationship between fear potential startle and anxiety is related to the size and state of the amygdala[8]. This new hypothesis is what prompted them to dive deeper about the size of the amygdala, just as Tuulari et al examined with newborns.

Tuulari et al found that there was a positive association between the magnitude of the fear potential startle and the severity of anxiety. However, there was also a negative association between the fear potential startle and the severity of anxiety with children diagnosed with autism spectrum disorder who also had smaller amygdalas[8]. Although this article uncovered a great deal about the fear circuitry, there will still need to be more tests to confirm the relationship between the amygdala, anxiety and fear potential startle and how they may be linked to the heterogeneity of amygdala development in individuals with autism spectrum disorder.

Rodents, just like humans, were also found to have an underlying innate fear involving unconscious emotional processing[9]. Ren et al found that implicit fear - or unseen stimuli - increased activity in the amygdala which suggests that a subcortical pathway underlies innate fear[9]. Finally, this study reaffirmed findings from previous studies establishing that the amygdala plays a crucial role in fear circuitry, and that the fear circuitry comprises subcortical and cortical regions. To further investigate the fear circuitry, Leal Santos et al, examined the effects of various different drugs such as propranolol, sotalol, and 4 - Hydroxytamoxifen on mice's fear circuitry.

This study found that propranolol induced a decrease in fear response at the prefrontal cortex, hippocampus, and amygdala levels of circuitry[10]. However, interestingly, they also found that propranolol does not affect anxiety like behavior, fear generalization, or remembering a non-fearful memory[10]. The reason behind propranolol being able to affect fear circuitry is because it alters connectivity between the hippocampus, prefrontal cortex, and the amygdala while simultaneously changing the correlations of memory tracing reactivation rates across regions of the brain[10]. It also decreases activity in the lateral amygdala and Infralimbic area while changing memory reactivation in the dorsal dentate gyrus and bilateral amyg-

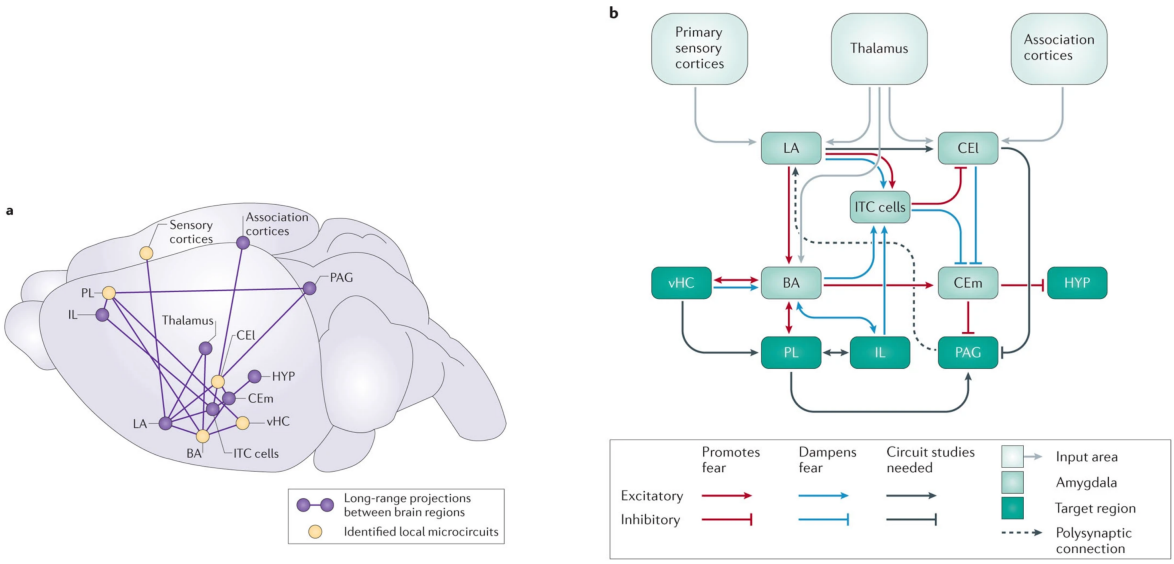

Fig. 1 The fear and extinction network. | **a)** Fear is determined by excitatory and inhibitory connections in the brain. **b)** Several amygdala nuclei receive sensory input from cortical and thalamic centres and are major sites of fear-related neuronal plasticity. This plasticity is modulated by reciprocal connections between the basal amygdala (BA) and the ventral hippocampus(vHC) as well as between the BA and the prelimbic cortex (PL). In turn, central nuclei of the amygdala project behaviour. Extinction of fear is mediated by different circuit elements within tt to hypothalamic and brainstem centres to promote fear of the same structures. Input from the infralimbic cortex (IL) to the BA and to the intercalated (ITC) cells is instrumental in dampening fear output from lateral central amygdala (CEl) nuclei to the hypothalamus (HYP) and the periaqueductal grey (PAG). The identity, connectivity and function of important forebrain-to-brainstem fear pathways remain to be characterized by modern circuit-based approaches. CEm, medial central amygdala; LA, lateral amygdala. Adapted from Tovote et al. 2015[6]

dala as well as changing the correlation between ACA, lateral amygdala, and dorsal cornu ammonis 3 - which are responsible for memory trace reactivation[10]. The results also indicate that propranolol affects fear retrieval but not innate anxiety of generalized fear[10]. Specifically, propranolol affects the dorsal dentate gyrus (dDG) but not other hippocampal subregions and this was mirrored in the prefrontal cortex when only the lateral amygdala was affected[10]. Similarly, in the amygdala, only the basolateral amygdala's (BLA) activation rate was altered due to propranolol. In the case of other drugs, it was found that sotalol did not decrease fear expression[10].

The results from this study are significant for patients suffering from post traumatic stress disorder. Propranolol only affects the connections between recalling a fearful memory, so it will not affect the other aspects of memory or fear, as shown by Santos et al. Propranolol did not affect anxiety behaviour, recalling non-fearful memories, or even fear in general - propranolol specifically targets fear retrieval and memory trace reactivation in specific parts of the brain[10]. These results suggest that propranolol could play a key role in creating a treatment for PTSD or other traumatic memory disorders.

The latest study on fear circuitry by Tao et al. had three goals: to see if there was a "core" neural network reflecting the fear processing in healthy individuals, which brain regions are recruited for fear processing at explicit and implicit conditions, and which brain regions are commonly and differentially activated for explicit and implicit fear processing. By using a meta-analysis of previous literature the study set out to find the neural signatures underlying fear processing.

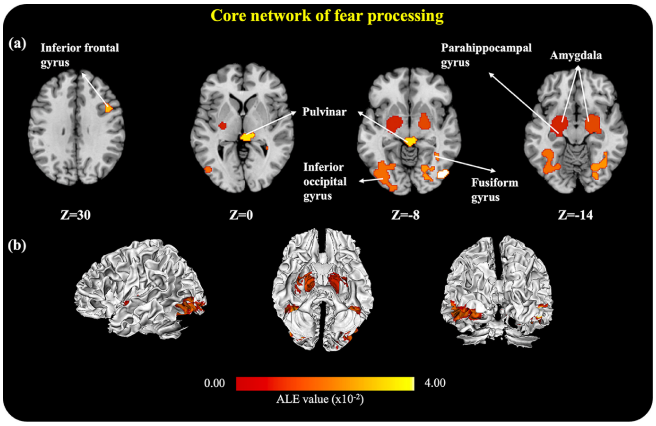

Fig. 2 The specific parts of the brain activated during implicit fear processing and explicit fear processing. Adapted from Tao et al. 2021[11]

The results found activations at the bilateral amygdala, right pulvinar, right inferior frontal gyrus, right middle

frontal gyrus, bilateral inferior occipital gyrus, and fusiform gyrus after finding studies with unconscious and conscious paradigms[11]. To take a broader perspective, it was found that fearful stimuli are processed in a network of brain regions symmetrically located on both hemispheres, including subcortical regions, such as the amygdala and pulvinar, and fronto-occipital regions, such as inferior frontal gyrus, inferior occipital gyrus, and fusiform gyrus[11].

Explicit fear processing (where the subject is aware of the fact that they are scared of the object) results revealed consistent activations at bilateral amygdala, right pulvinar, left parahippocampal gyrus and hippocampus, and fronto-occipital regions, including inferior frontal gyrus, middle frontal gyrus, inferior occipital gyrus, and fusiform gyrus[11]. Whereas, implicit fear (which is also the exact opposite of explicit processing as the subject does not know what it is scared of until it gets scared) results revealed greater activations at the left amygdala, left inferior parietal lobule, left inferior frontal gyrus, and bilateral inferior occipital gyrus[11].

Both, implicit and explicit fear processing, use the bilateral amygdala, left declive and fusiform gyrus, and right middle frontal gyrus[11]. There is a huge overlap at the bilateral amygdala which suggests a shared neural substrate as both the left declive and fusiform gyrus, and right middle frontal gyrus are activated for both types of fear[11]. This study also found that the amygdala is important for fear processing regardless of the level of awareness or type of stimuli as it has extensive connections with the cortical areas (visual cortex and prefrontal cortex) as well as the subcortical areas (pulvinar)[11].

A unique idea unexplored previously is the cerebellum being essential to the neural circuits regarding emotion and affect - particularly, fear related processes. However, what has been stated multiple times is the left amygdala's activation during fear - especially, during implicit fear but not during explicit fear. This is replicated when the parahippocampal gyrus is activated during explicit fear compared to when implicit fear is activated[11]. This phenomenon is explained by the fact that the parahippocampal gyrus plays an important role in contextual processing and associates emotion with context cues[11].

Surprise

One of the 6 core facial expressions that can be recognized in the human neural system is the expression of surprise[12]. Surprise remains somewhat mysterious, as relatively little has been discovered about its neural circuitry. In fact, it wasn't until the early 2000's that scientists were able to make bigger strides in studying its importance. What separates surprise from fear is the fact that surprise can have positive connotations as opposed to fear's constant negativity. Even better, surprise circuitry has been found to overlap with other circuitries

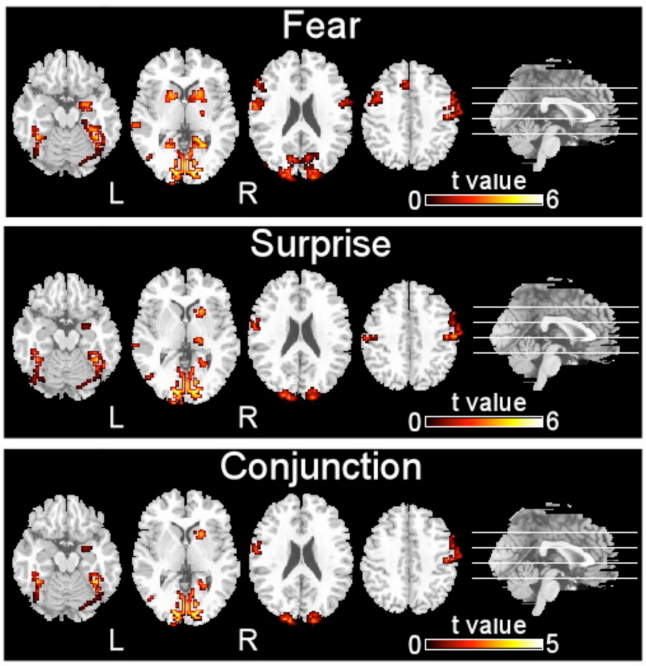

Fig. 3 Fear and surprise activate both shared and independent brain regions. Adapted from Zhao et al. 2017[3]

- such as learning - which shows how surprise can offer many new insights into human lives 13 .

Previous work in the field has found that the amygdala and the prefrontal cortex played vital roles in the circuitry[13]. This work laid the foundation into investigating the emotion of surprise, and began the basis of discovering exactly how the amygdala and the prefrontal cortex contributed to the dense neural circuitry. To properly examine the connection between the amygdala and the prefrontal cortex, Kim et al used stimuli on subjects to assess the responsivity to positively and negatively cued surprises and also used functional magnetic resonance imaging scans to model the amygdala's responses. The ability to separate positivity and negativity of surprise was a key role in the investigation and allowed them to dissect different brain regions activated during negative and positive surprise reactions. They used phrases to separate between the two types of surprise reactions : he/she just lost $500 and he/she just found $500. Along with the phrases, there was also an image of a surprised face that was given.

The results revealed that there was a clear and distinct match for which brain region associated with a positive surprise and which region associated with a negative surprise as well as whether a sentence or a face activated the amygdala. The amygdala had an integral role to play as it was found that negatively versus positively cued faces and stimuli faces in general, cued a greater left ventral amygdala activation[13]. On the

other hand, the sentences led to a greater activation in the prefrontal cortex [13]. The right ventrolateral prefrontal cortex had a greater activation with negative versus positive sentences and the right ventromedial prefrontal cortex had a greater response for positive versus negative sentences [13].

Even more, there was a clear relationship with the amygdala and prefrontal cortex in some scenarios [13]. When the ventral amygdala was activated for negatively cued faces, there was a positive correlation within the dorsomedial prefrontal cortex which mirrors when the ventromedial prefrontal cortex was activated in response to positive sentences, there was a positive correlation with the dorsomedial prefrontal cortex [13]. Similarly, the ventrolateral prefrontal cortex's response to negatively cued sentences had a positive correlation with the dorsomedial prefrontal cortex and the ventral amygdala while also having a negative correlation with the ventromedial prefrontal cortex [13].

The discovery of distinct positive and negative surprise circuitries truly reveal how complex the emotion is. The emotion is so complex, in fact, it shares its circuitries with other circuitries as well [14]. As we continued to gather more knowledge on the neural circuitry behind surprise, Betzel et al expanded the knowledge on the subject by comparing the surprise circuitry to the circuitry of learning. By using data from the MyConnectome Project - an extensive neuroimaging data set of a single subject's brain acquired over 34 years - Betzel et al was able to track the subject's mood and the subject's level of surprise which he then mapped out as data.

The results of this study confirmed that surprise and learning both, unsurprisingly, share many of the same neuronal circuitries [14]. The study explored in depth how surprise and network flexibility in the brain are negatively correlated, showing how the less surprised an individual becomes, the more they learn and the better their adaptability to stimulus is [14]. This was interesting to see as we now know that depending on the specific brain's flexibility, some may find it harder to learn as their surprise circuitry may be damaged in the amygdala - which is known to affect the circuitry 14 - which inhibits their network flexibility in their brain [14]. This also works vice versa where if the learning circuitry is damaged then the surprise a person feels may be greater -or less depending on the specific region of the damage [14]. Essentially, it is the brain flexibility that determines whether a person will have a surprised response or not [14].

The implications of this study were significant towards helping to fix learning disorders such as ADHD and dyslexia as we learn more about the neural circuitries and how they interconnect. One of the 6 core facial expressions that can be recognized in the human neural system is the expression of surprise [3]. In Zhao et al, researchers used sets of functional magnetic resonance imaging scans to determine precisely which region of the brain increases in activity after a participant is subjected to stimuli.

First and foremost, this study identified a surprised facial expression as one with a raised inner and outer brow, raised eyelids, and open mouth. These expressions also had to convey unexpectedness and novelty. Participants of the study were shown a face and told to identify the face as either having a surprised look or fearful look. The participant's facial responses were then correlated to the functional magnetic resonance imaging scans. They identified the activated parts of the brain in response to surprised to be: left postcentral gyrus, left middle occipital gyrus, left supplementary motor area, lentiform nucleus, right calcarine, right postcentral gyrus, right precentral gyrus, right inferior occipital gyrus, right parahippocampal gyrus, and the right amygdala [3]. In essence, the temporal and occipital cortices are active for surprise circuitries. A big positive for this study is how detailed and comprehensively Zhao et al covered various brain regions that are involved in the circuitry.

One interesting finding is that the parahippocampal gyrus is comprehensively activated for both consciously and unconsciously perceived surprise [3]. Although the right parahippocampal gyrus and the amygdala did increase activity for surprise, they are also activated in fear, suggesting that these regions of the brain are not unique to surprise circuitry and affect other emotions as well. Finally, a very key difference that this study found between fear and surprise was that surprise brings out emotion and fear does not. This shows another aspect where the surprise circuitry overlaps with another set of circuitries [3].

From the latest studies investigating the surprise circuitry, this was the first to test whether surprise actions and surprise inhibition both recruit the fronto-basal-ganglia. One of this study's unique methods was that it was the first study to use functional magnetic resonance imaging to test whether surprising events recruited the fronto-basal-ganglia. They were able to test both unexpected action and unexpected inhibition in one experimental design, which had never been done before. These tools allowed them to test for condition-specific neural signatures and the task's design allowed them to study surprise as a form of reactive inhibition in neuropsychiatric patients with inhibitory deficits. The premise of the experiment was to see if the participants - with speed and accuracy - would respond to stimuli as expected.

The low error rates from the participants showed that both unexpected action and unexpected inhibition recruit the fronto-basal-ganglia. The fronto-basal-ganglia network consists of cortical activity in the right inferior frontal gyrus/anterior insula and presupplementary motor area and subcortical activity in the right subthalamic nucleus region and caudate nucleus [15]. Even more, the degree of surprise positively correlates with the change in the subthalamic nucleus which indicates that the more the subthalamic nucleus is ac-

tivated, the stronger the event affects action and cognition [15]. This was backed up in the experiment when the subjects took a longer time to respond to the stimuli when it was more surprising. Meta-analysis from this study linked surprise to a network comprising of the inter alia, the right anterior insula and right inferior frontal cortex, midcingulate cortex/presupplementary motor area, dorsal striatum, inferior parietal lobule and middle temporal gyrus [15]. Along with all the brain regions, this study also found that the surprise circuitry shares much with the reinforcement learning circuitry [15].

Discussion

Both the emotions of surprise and fear have recently been studied in depth as scientific technology advances. Naturally, there remains many more exciting discoveries to be made regarding these two emotions and their circuitries. Present studies show some ambiguity between the words 'fear' and 'surprise'. Zhao et al indicated this ambiguity when they attempted to define what expressions of surprise and fear would look like with specific details such as a raised brow and open mouth. Unfortunately, there is no uniform look for an expression of fear or surprise that all humans interpret the same way. This ambiguity is an important reason to keep researching fear and surprise to find better ways to redefine these expressions and obtain more accurate results.

The emotion of fear has been studied more extensively, and has more comprehensive data compared to the emotion of surprise. However, there is still much work to be done to confirm many theories, and a long way to go in finding all regions of the brain that are involved in the neural circuitry. This was shown in Pitcher et al when it was discovered that transcranial magnetic stimulation did not affect expression identification which led to even more experimentation [16]. However, is the orbitofrontal amygdala the only pathway for expression identification or is there another set of circuitry that has this function? A future study that includes conducting the experiments bilaterally with transcranial magnetic stimulation may shed light on what regions of the brain are necessary versus sufficient in triggering the appropriate fear responses.

As for the emotion of surprise, there is a plethora more to be uncovered about its circuitry. Out of the many brain regions found to be a part of surprise, only the prefrontal cortex and the amygdala have been thoroughly studied in detail. The rest of the pathway has not been entirely found nor the other known regions thoroughly investigated, leaving plenty of room for future discoveries. In Sebastian et al we did find that the surprise circuitry overlaps with the reinforcement learning circuitry, but that study has only helped us to learn more since then - we must build on this foundation and dig deeper [15]. Compared to the literature on fear circuitry, there is a much bigger gap in our knowledge of the surprise circuitry that remains to be filled. Thankfully, the existing literature will help make the process easier and inspire the future. An important study to be conducted in the near future would be to understand the patterns of network modulations and their relationship to mood along with going into more detail about why decreased surprise is accompanied by increased network variability, as Betzel et al recommended.

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References

1 T. Zhang, *The Meducator*, 2014, **1**, year.
2 H. Damasio, *Revue Neurologique*, 2018, **174**, 738–739.
3 K. Zhao, J. Zhao, M. Zhang, Q. Cui and X. Fu, *Frontiers in Psychology*, 2017, **8**, 761.
4 R. Adolphs, D. Tranel, H. Damasio and A. Damasio, *The Journal of Neuroscience*, 1995, **15**, 5879–5891.
5 J. J. Tuulari, E.-L. Kataja, J. M. Leppänen, J. D. Lewis, S. Nolvi, T. Häikiö, S. J. Lehtola, N. Hashempour, J. Saunavaara, N. M. Scheinin, R. Korja, L. Karlsson and H. Karlsson, *Developmental Cognitive Neuroscience*, 2020, **45**, 100839.
6 P. Tovote, J. P. Fadok and A. Lüthi, *Nature Reviews Neuroscience*, 2015, **16**, 317–331.
7 F. Celik and I. S. Edipoglu, *European Journal of Medical Research*, 2018, **23**, 41.
8 D. Hessl, L. Libero, A. Schneider, C. Kerns, B. Winder-Patel, B. Heath, J. Lee, C. Coleman, N. Sharma, M. Solomon, C. W. Nordahl and D. G. Amaral, *Autism Research*, 2021, **14**, 450–463.
9 C. Ren and Q. Tao, *Advances in Experimental Medicine and Biology*, 2020, **1284**, 1–7.
10 S. L. Santos, M. Stackmann, A. M. Zamora, A. Mastrodonato, A. V. D. Landri, N. Vaughan, B. K. Chen, M. Lanio and C. A. Denny, *Biological Psychiatry*, 2021, **89**, 1150–1161.
11 D. Tao, Z. He, Y. Lin, C. Liu and Q. Tao, *NeuroImage*, 2021, **227**, 117686.
12 A. S. Cowen, D. Keltner, F. Schroff, B. Jou, H. Adam and G. Prasad, *Nature*, 2021, **589**, 251–257.
13 H. Kim, L. H. Somerville, T. Johnstone, S. Polis, A. L. Alexander, L. M. Shin and P. J. Whalen, *Journal of Cognitive Neuroscience*, 2004, **16**, 1730–1745.
14 R. F. Betzel, T. D. Satterthwaite, J. I. Gold and D. S. Bassett, *Scientific Reports*, 2017, **7**, 520.
15 A. Sebastian, A. M. Konken, M. Schaum, K. Lieb, O. Tüscher and P. Jung, *The Journal of Neuroscience*, 2020, **41**, 2447–2456.
16 D. Pitcher, L. Garrido, V. Walsh and B. C. Duchaine, *Journal of Neuroscience*, 2008, **28**, 8929–8933.