BME 201 (Biomedical Engineering Design)
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Project #13: Development of a Device for Neurochemical Sample Collection from Freely Moving Monkeys

FINAL REPORT

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Abstract

The goal of this design project is to develop and construct a device to provide protection for the microdrive unit, an apparatus which is used in microdialysis experiments conducted on non-human primates. This would allow the experiments to be conducted without restraining the monkeys in a chair, providing them with a more comfortable and realistic experimental setting. Currently, there are no existing devices in the market specifically catered for this purpose. In accordance with the client's requirements, the team considered three design alternatives, and ultimately chose to pursue the Cushion and Shell design. Based on the design, the team began construction of an aluminum casing with a form-fitted foam interior to surround the microdrive unit. In the future, the team seeks to further modify and improve on the device, and then submit it for approval for preliminary testing on monkeys.

Problem Motivation

Microdialysis allows for real-time *in vivo* measurements of various substances in the body[2]. In particular, direct measurements of neurochemical substances in the brain from free-moving non-human primates is significantly important for understanding complex brain function and developing treatment strategies for brain disorders in humans. A modified microdialysis method has been developed for application to Rhesus macaques (*Macaca mulatta*). However, it requires restraining the monkeys in chairs for up to 12 hours while samples are collected. Although this is considered a norm and the monkeys have been appropriately conditioned, the situation is less than ideal since the monkeys are subjected to a certain amount of discomfort due to the restricted movement and long period of chairing. The data collected might also not be representative of a monkey in its natural environment, since it is confined to a chair. One way to address this problem is to allow the monkeys to be free from chairing while the experiments are being conducted. Besides alleviating the discomfort experienced by the monkeys, it would also better simulate the monkey's natural environment since it would be free to move around, albeit within the confines of a cage. Additionally, this method would allow the experiments to be conducted without the 12-hour limit imposed by chairing. More time would be available for sample collection and safety inspections to be conducted, allowing the experiments to be carried out more smoothly and safely. However, allowing the monkeys to move freely introduces the risk of them tampering with the experimental apparatus (called a microdrive unit), thus compromising the experimental procedure. Hence, a protective device must be constructed to protect the microdrive unit during the experiment. This device must be compatible with the monkeys such that it will not incur greater discomfort than is necessary or encumber the experimental process. There are currently no products in the market that specifically address this issue, so a suitable device must be designed and constructed.

Background

RHESUS MACAQUE

The Rhesus macaque, also known as the Rhesus monkey, is one of the best known species of Old World monkeys. Rhesus macaques have an extensive geographic distribution and are found ubiquitously throughout mainland Asia, ranging from Afghanistan to India and Thailand to southern China. They range in color from brown to grey and have little fur, if any, on their reddish-pink faces[5]. On average, adult males measure approximately 53 cm and weigh 7.7 kg. Females are smaller, measuring 47 cm and weighing 5.3 kg on average. Their tails are of medium length, averaging between 20.7 and 22.9 cm, and are not prehensile (i.e. the tails are not adapted to be able to grasp and/or hold objects). Typically, Rhesus macaques have a lifespan of about 25 years[10].

Because of their anatomical and physiological similarity to humans, as well as the relative ease at which they can be maintained and bred in captivity, Rhesus monkeys have long been an ideal choice to carry out research on non-human primates. As a result, they have become the most studied non-human primate, both in the field and in laboratory settings. Examples of research involving Rhesus monkeys include the development of rabies, smallpox, and polio vaccines, and the creation of drugs to manage HIV/AIDS[5]. As with all other macaques, the *Herpesvirus simiae* (B virus) is endemic among Rhesus monkeys, but could be deadly if spread to a human. Thus, extra care must be taken when interacting with them.

CLIENT'S RESEARCH

A faculty member at the University of Wisconsin-Madison Department of Pediatrics, the client is interested in understanding how growth and development are controlled in humans. One particular focus is on the role of the brain in triggering puberty[3, 4]. In order to investigate this, the client studies neuroendocrine function by measuring the release of neuropeptides, neurotransmitters, and neuromodulators from the hypothalamus in the brain. Currently, this research is being carried out on Rhesus monkeys, due to their anatomical and physiological closeness to humans. It is hoped that through these neuroendocrine studies on the monkeys, a better understanding of complex brain function in humans can be achieved. Since the studies revolve around the events occurring during puberty, the monkeys used for the experiments are generally young and pubertal. Unlike adult Rhesus monkeys, these monkeys generally range from 2.5 to 5 kg in weight[1].

MICRODIALYSIS & EXPERIMENTAL PROCEDURE

In order to study the release of substances from the hypothalamus of the Rhesus monkeys, a technique known as microdialysis is employed. Microdialysis is widely used in clinical research in areas such as neuroscience (to study the neurochemical bases of brain disorders) and pharmacology (to study drug metabolism, drug delivery, and the effects and efficacy of drugs) [6]. In general, microdialysis entails inserting a probe into the extracellular fluid of a particular part of the body. The probe contains a semi-permeable membrane for substances to diffuse in/out based on a concentration gradient. The inlet of the probe is connected via tubing to a pump which infuses a physiological salt solution. Exchange of substances occurs at the semi-permeable membrane, and the desired samples are collected by a fraction collector connected via tubing to the outlet of the probe[2, 9].

A brief outline of the experimental setup used in the client's research is shown in Figure 1. Before experiments can be conducted on the monkeys, a cranial pedestal (head cap) must be implanted into their skulls and secured using dental cement and screws. This allows the microdrive unit to be fitted onto their heads. The purpose of the microdrive unit is to properly position the microdialysis probe for insertion. On the day of the experiment, the monkey is anesthetized and placed in a stereotaxic apparatus. The microdrive unit with a guide cannula are attached and positioned precisely to the specific area desired for testing. Accurate placement is ensured using radiographic visualization. The monkey is then transferred to a primate chair (Figure 2), which it has been conditioned and well-adapted to prior to the experiment. Apart from moving its hands to feed itself and turning its head a little, all other movements of the monkey are restricted by this chair. Once the monkey has been put in place, the guide cannula is removed and the microdialysis probe is inserted. The pump is used to perfuse cerebrospinal fluid (CSF) through the probe and the exchange of substances occurs at the semi-permeable membrane (which is in the vicinity of the hypothalamus). The perfusate containing the desired substances which have diffused into the probe are collected by a fraction collector and immediately frozen for storage. The entire experimental process takes approximately 12 hours, and the monkeys are confined to the chair throughout this time[1].

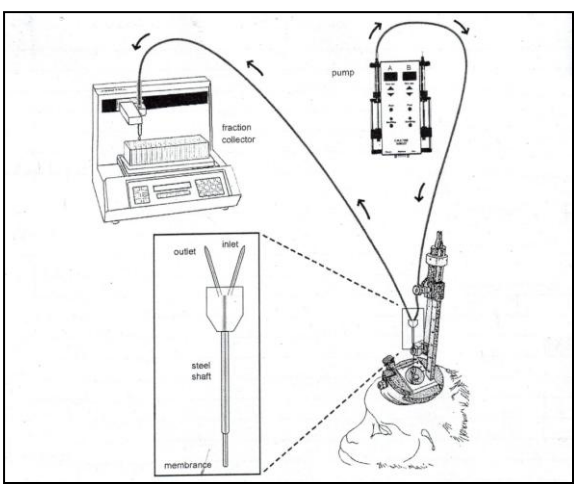

Figure 1: Experimental Setup for Microdialysis[1]

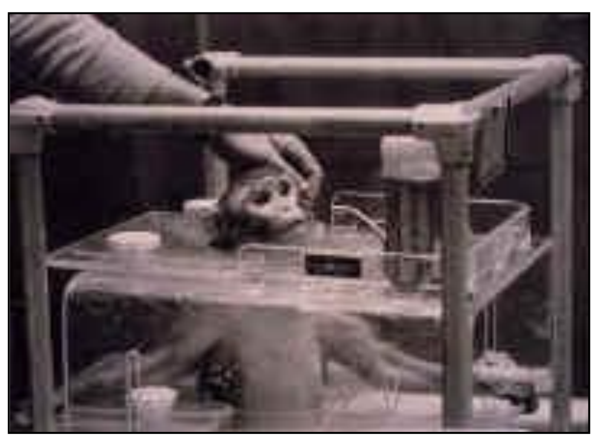

Figure 2: Rhesus Monkey in a Primate Chair[8]

Client's Requirements & Design Constraints

The device must be strong enough to provide protection for the microdrive unit such that the monkeys will not be able to tamper with it during the experimental process. This means that the device must be rigid and cover the entire microdrive unit. Taking into account any forces that the monkey may apply, it should also be able to withstand a force of 100 N. This value was an estimate based on human arm strength[7].

Given that the monkeys are generally smaller in size than the average adult Rhesus monkey, the microdrive unit already imposes a considerable amount of weight on the monkey's head. As such, the materials used to construct the protective device must be lightweight (not more than 0.5 kg, which is an estimate determined by the client based on prior experience with working with Rhesus monkeys) to minimize the additional weight to be imposed.

The design of the device must be simple such that it can be easily integrated with the current experimental apparatus, so as not to interfere with or impede the data collection process. Yet, a certain degree of complexity must be incorporated to prevent the monkeys from dismantling the device. Also, there must not be any sharp edges or protrusions that can possibly harm the monkey or researcher during the experimental setup and process.

The device should be detachable by the researcher, so that adjustments to the experimental apparatus can be made during the experiment if needed. This will also allow the device to be cleaned and sterilized prior to subsequent use. In addition, the design and construction of the device must comply with USDA regulations and NIH guidelines, subjected to approval by the attending veterinarian.

Design Alternatives

JACKET & METAL RING

The first possible design is the Jacket & Metal Ring design (Figure 3). This would comprise a nylon fabric mesh jacket, an attached metal pole that extends up from the back of the jacket, and a metal ring (attached to the top end of the metal pole) that fits tightly around the monkey's head. Additionally, there would be a protective metal dome welded to the ring that covers the base of the microdrive unit, and a PVC tube to cover the upper portion of the microdrive unit. Since the monkey's head has to be restrained vertically, nylon straps would be used around the chin and neck to prevent the monkey from moving its head.

Currently, mesh jackets that have been designed to fit the monkeys are available. They fit like a T-shirt with short sleeves and a hole for the neck. They are secured with two, layered zippers on the back making it difficult for the monkey to escape. However, the jackets are not very tight-fitting, and the monkeys have been known to be able to maneuver the jackets on their bodies, to the extent of flipping them around such that the jacket is on backward. Placing an additional strap around the monkey's abdomen will prevent the pole and ring device from bending away from the monkey's head or body.

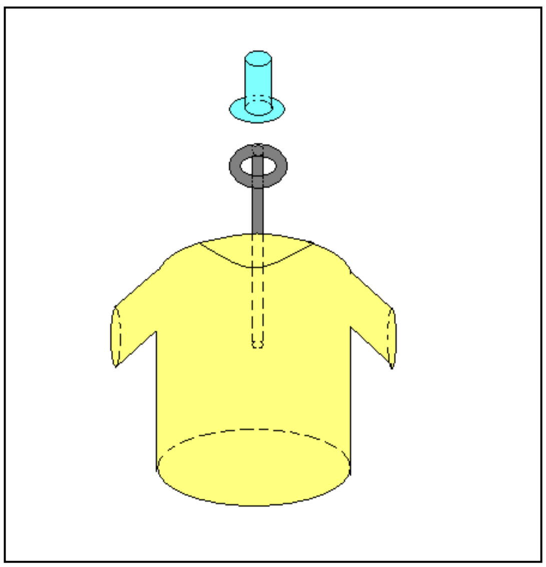

Figure 3: Jacket & Metal Ring Design

A metal rod will then attach to the jacket and extend up to the monkey's head. This rod will be secured to the jacket in an additional sleeve, which can be sewn directly onto the back of the jacket. The rod will extend along the back and be attached to a metal ring that sits atop the monkey's head. The ring will be interchangeable with other rings in order to fit monkeys with different head sizes, and will fasten to the rod with an Allen screw. The monkey's head will be locked into place next to the rod and ring by nylon straps. Two straps will extend down from the ring around the monkey's chin, and a third strap, connected at the chin to the first two, will wrap around the neck and connect to the metal rod. This will prevent the monkey from turning or moving its head during the experiment.

On top of the ring, a metal dome with a hole in the top will be welded to the ring. The dome will encompass the entire base of the microdrive unit and extend down to the metal ring. It will not touch the microdrive unit or the monkey, but only be secured to the metal ring around the monkey's head. The PVC cylinder will then fasten to a hole at the top of the dome. This protects the top part of the microdrive unit. The PVC will also connect to the tether that houses the tubing.

This device would need to be put on in two stages. First, the jacket would be secured on the monkey before it is anesthetized. Then, after the microdrive unit has been attached, the ring and rod device would slide down atop the whole monkey with the tethered connection being made after the microdialysis probe has been inserted.

Advantages to this design are that the weight of the device is distributed throughout the monkey's body and that the housing apparatus is very durable. The pole connected to the rest of the device distributes the weight around the abdomen through the abdominal strap. The head straps are mainly to prevent movement of the monkey's head down and out of the metal ring. The device can be heavier because the weight is distributed. This allows the rest of the housing to be made of more durable metals.

The disadvantages are that the mesh jackets are not tightly secured to the monkey's body. This means that the monkeys are able to slip around inside the jackets and stretch them in places. They have also been known to pick at the zippers in order to escape. Also, the experimental procedure while the monkey is anesthetized is quite rushed, and the jacket takes a while to put on. Adding the metal rod, ring, and straps may cause the procedure to take too much time for this option to be viable.

HELMET

The second alternative is the Helmet design (Figure 4). It resembles a bicycle helmet with a PVC pipe sticking out at the top. It is the most simple of the three designs and has only three main components: PVC cylinder, dome helmet, and straps.

The main part of the helmet will be made out of carbon fiber. Carbon fiber is lightweight and very strong, so it will be good for protecting the monkey without adding too much extra strain to the monkey's neck. The helmet will have an inner rim, which rests closer to the head cap and provides additional support and friction to help the helmet stay centered on the head. The helmet will cover the entire base of the microdrive unit with its dome shape, and have a hole at the top for the upper portion of the microdrive unit.

The upper portion will be a PVC tube similar to that used in the Jacket & Metal Ring design. It will cover the upper portion of the microdrive unit. Again, it connects to the hole at the top of the helmet and to the tether through which the sampling tubes are passed. The entire device stays on the head mainly due to straps around the chin and neck. Nylon straps, tightened at the helmet, will extend down and around the chin. These straps will then be connected to another strap that wraps around the neck to the back of the head and connects from there to the back of the helmet. The latter strap prevents the monkey from pulling the former straps up far enough to get them into its mouth and possibly chew on them.

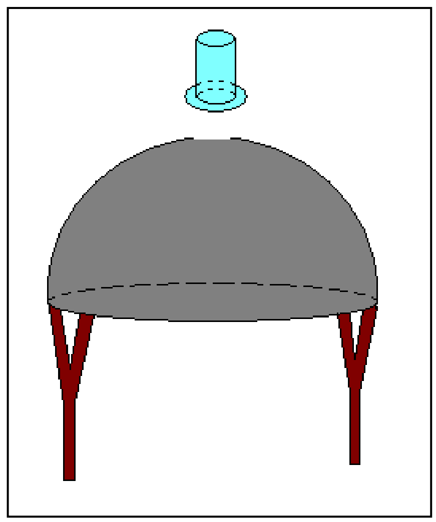

Figure 4: Helmet Design

After the microdrive unit is secured and the sampling tubes have been inserted, the helmet will slide over the top of the monkey's head. The PVC tube will be attached to the tether, but can slide along it and be removed for cleaning. The entire helmet device will be secured to the tether so that it can no longer slide along the tether.

One advantage of this design is that it is very simple. The design only has 3 different parts and the helmet and PVC portions are both very easy to make. The straps may be a bit more difficult to engineer, but all three designs have a similar component, so this is not a disadvantage when compared to the other two. Also, it is the smallest and lightest of the three designs.

Unfortunately, the straps alone may not be enough to keep the helmet from sliding around on the monkey's head. If the helmet can move enough to touch the protective device, this design would not achieve its intended purpose. Also, fastening of the PVC to the tether during the experimental set up would take some time, and this might deter the researchers from wanting to use it.

CUSHION & SHELL

The third design alternative is the Cushion & Shell design. This design is composed of three hard outer casings that surround a soft inner core. The protective device is secured to the head of the monkey by nylon straps that attach to the outer casing and extend around the monkey's chin. The three outer casings, made from aluminum, provide protection to the microdrive unit. The soft inner core, made from a polymer, provides added protection to the microdrive unit in addition to providing stability to the protective device.

The base of the microdrive unit will be protected by two half disks. A representation of one of the half disks is shown in Figure 5. The two half disks will be attached together by Allen screws allowing the protective device and the soft inner core to be placed on the monkey's head after the microdrive unit is already in place. This is important because there would be no way to insert a soft inner core into the outer shell if the two half disks were fused into one piece. Lastly, nylon straps will attach to the outside of the two half disks and extend down and around the monkey's chin to secure the casing to the forehead of the monkey. Additional straps will be used as necessary to prevent the monkey from biting through the nylon straps.

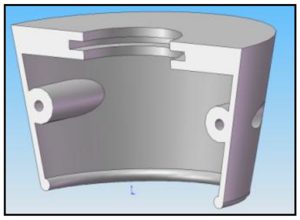

Figure 5: Half Disk

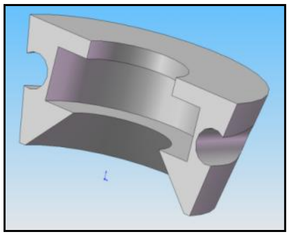

Figure 6: Soft polymer core

The soft inner core lies within the two outer casings that protect the base of the microdrive unit. It will be made up of a polymer that is molded to the inside surface of the hard outer casing. In addition, the soft inner core will have a cavity within it that is molded to the shape of the base of the microdrive unit (Figure 6). The soft inner core provides additional protection to the microdrive unit by padding the microdrive unit from the hard outer shell. Also, the cavity that is molded to the shape of the microdrive unit helps to keep the entire protective device correctly aligned on the monkey's head.

The upper cylindrical shell protects the remainder of the microdrive unit. It will simply be a cylindrical shell constructed from aluminum that has a lip on one end and an attachment for the tether at the other end (Figure 7). The lip will fit perfectly within the slots that are machined into the top of the two half disks. The lip-groove relationship secures the upper cylindrical shell to the other two half disks when the disks are fastened together using an Allen screw. The tether, on the other hand, will be attached to the cylindrical shell directly using multiple Allen screws. A representation of the entire Cushion & Shell Design is shown in Figure 8.

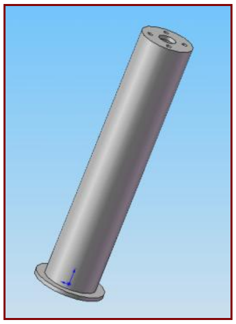

Figure 7: Cylindrical Shell

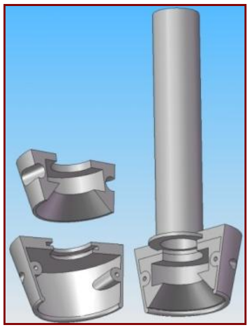

Figure 8: Cushion & Shell Design

The advantages of this design include its soft inner core and its ability to clamp around the microdrive unit. The two half disks that clamp around the microdrive unit allow a soft inner core that is molded to the shape of the microdrive unit to be imbedded within it. The soft inner core provides additional protection to the microdrive unit that is lightweight, and it also helps to keep the protective device correctly aligned on the monkey's head.

Disadvantages of the Cushion & Shell design include its complexity and how it distributes its weight onto the monkey. The complexity of this design comes from the three hard outer casings, the soft inner core, the various nylon straps, and the Allen screws. This could make construction of this design very challenging. Also, this design puts all of its weight on the head of the monkey instead of distributing it to other areas of the monkey. Consequently, the protective device would need to be constructed out of a lightweight material that would reduce the strain on the monkey's head.

Design Matrix

In order to evaluate the three design alternatives, a design matrix was created with several weighted criteria and the designs were ranked in each category (Table 1).

The first criterion is security from the monkey. Monkeys are very clever animals capable of fine motor movements. As a result, the monkeys must not be able to unscrew the device, take it off, or otherwise interfere with the function of the system. For the first design, the available jackets are made of a mesh material and have many zippers. With this setup, the monkeys have been able to chew on the mesh and undo some of the zippers, which would not make the device very secure from the monkey. However, both the Helmet and Cushion & Shell designs are secured by straps and Allen screws. This system is much more difficult for the monkey to interfere with since they cannot undo things put together with Allen screws and the straps will be under the chin and neck preventing them from putting the straps into their mouth.

Another important factor in the design is the security from slip. While the device is on the monkey's head it cannot move around and forcefully hit the microdrive unit and knock it out of place. For the Jacket & Metal Ring design, the jacket does not fit tightly on the monkey's body, so it is likely that it would cause the entire device to slip since the device is anchored by the jacket. The Helmet design is anchored by straps which would be a more stable securing point, and the Cushion & Shell design has the straps along with the close molding to provide more support.

The ability of the device to withstand force is a key aspect of the designs. Rhesus monkeys are strong and capable of hitting the device with their hands or on the side of the cage. As a result, the device must be able to withstand these forces without breaking. All of the design alternatives were ranked the same for this criterion since all have the same cylinder column extending up over the microdrive unit, which is the main piece that will need to withstand force. The ranking was also quite high since the materials planned to be used (PVC or aluminum) are both strong materials.

Ease of use is a less important component of the designs, but still is something that needs to be taken into consideration. It would be ideal to have the monkeys anesthetized for the least amount of time possible and the researchers have a lot on their minds when conducting the experiment, so creating a system that is easy to implement is important. The Jacket & Metal Ring design has a lot of different parts that would be hard to put on the monkey. A jacket with a metal rod, ring, and dome attached to it would be very difficult to maneuver. The Cushion & Shell design would be easier to use since it involves less parts and only has attachments on the head. The easiest to use would be the Helmet design since the researchers would just need to strap it on and pull down the protective PVC cylinder.

Another criterion is the ease of construction. The chosen design must be constructible so it can be used by the client and possibly reproduced if successful. The Jacket & Metal Ring design involves many different pieces, creation of metal parts, welding, and attachments to different jackets for different size monkeys. All of this is quite complex and would be difficult to create. The Cushion & Shell design would be easier to create since it involves fewer parts; however, specialty metal parts need to be made which adds difficulty to its manufacturing process. The Helmet design would overall be the easiest to create, but there would be challenges in finding how to create a helmet that would appropriately fit the monkey's head.

Safety is the last criterion used to decide among the design alternatives. A checkmark system was used for this factor since any device that is chosen to be pursued must be safe for both the monkeys and the researchers. It cannot be toxic, have sharp edges, or involve small pieces that may fall off. All of the design ideas received a checkmark for this category since they do not involve any of the aforementioned concerns.

	Jacket & Metal Ring	Cushion & Shell	Helmet
Security from Monkey (30)	15	18	18
Security from Slip (20)	7	15	10
Ability to Withstand Force (30)	25	25	25
Ease of Use (10)	3	7	8
Ease of Construction (10)	3	5	6
Safety	✓	✓	✓
Total	**53**	**70**	**67**

Table 1: Design Matrix

When the numbers of the design matrix were added together, the Cushion & Shell design came out on top. The team chose to pursue this design not only due to the analysis using the design matrix, but also because it intuitively seemed to be the design that would allow for the most support and protection of the microdrive unit. The entire device would be relatively secure from the monkey with the Allen screws and strap system. It would also be stable on the monkey's head, since it is secured by both straps and the tight molding. The aluminum is very strong and would allow for the device to withstand large amounts of force. Lastly, the device would be easy enough to use and construct, although there might be some challenges.

Final Design

The final design is a modification of the preliminary Cushion & Shell Design. This design is composed of three aluminum pieces that fit together to enclose the microdrive unit. Two aluminum half shells containing a soft, form-fitted foam interior surround the base of the microdrive unit. The foam interior provides stability and cushioning for the microdrive unit. The third aluminum component extends above the base and surrounds the rest of the microdrive unit. Figures 9 and 10 illustrate the aluminum components of the final design. The two aluminum half shells are cut in such a way to provide a custom fit for a Rhesus monkey. The dimensions used for the final design are shown in Figures 11 and 12.

All three aluminum components are then held together simply by using a hose clamp (Figure 13). To protect the small tubing used for microdialysis, a tether is attached to the top aluminum piece and extends up to the top of the cage. In addition, nylon straps extend around the chin and neck from the bottom of the two half shells.

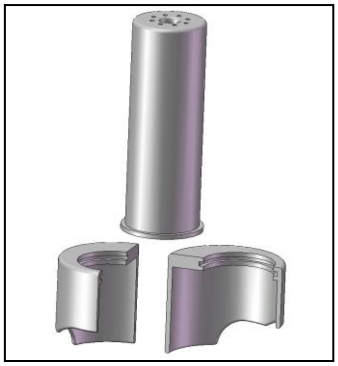

Figure 9: Components of the Final Design

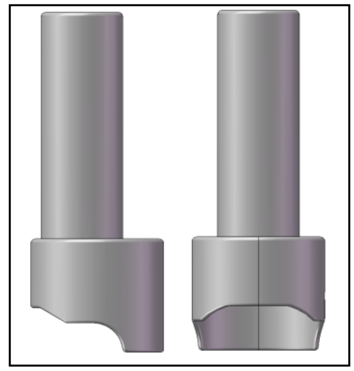

Figure 10: Complete Final Design (Side and Front View)

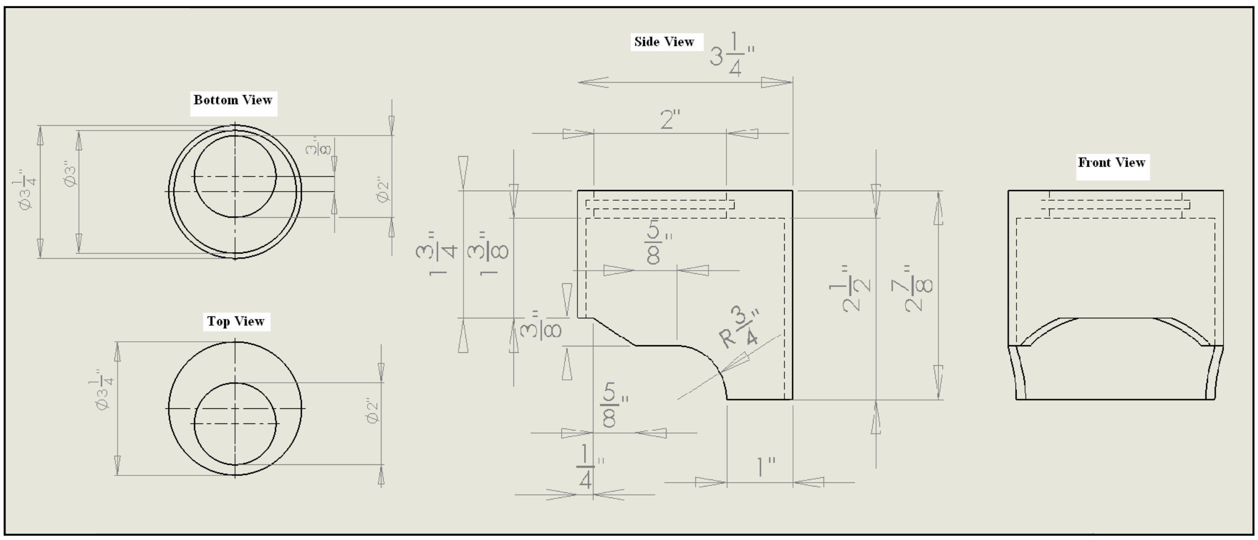

Figure 11: Dimensions for the Base of the Final Design

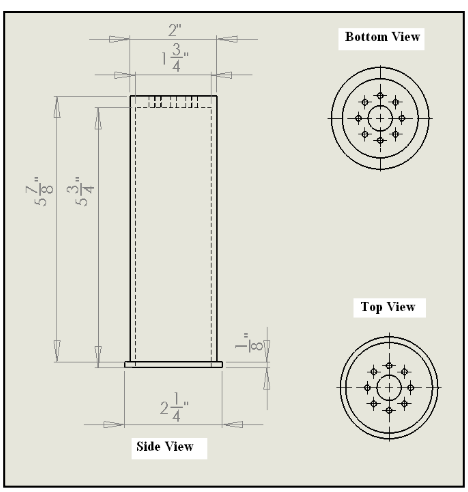

Figure 12: Dimensions for the Top of the Final Design

Figure 13: Hose Clamp

Due to certain limitations, the aluminum prototype was unable to be completed. Specifically, the base of the prototype was not cut to provide a custom fit for a Rhesus monkey and the foam interior was not added. The current aluminum prototype is shown in Figure 14. Instead, a polyvinyl chloride (PVC) prototype was constructed to act as a model of the desired aluminum prototype. PVC is a conservative alternative to aluminum because it provides similar strength and durability. The density of PVC (1380 kg/m³) is lower than that of aluminum (2685 kg/m³). However, the thickness of PVC used was 0.25 inches, which is twice that intended for the aluminum prototype. Hence, the volume of the PVC prototype would be more than twice that of the aluminum prototype. Using this estimate, and the density values, the weight of the PVC prototype would be greater than that of the aluminum prototype. In addition, for construction purposes, PVC is much easier to manipulate because it can be glued and cut relatively easy. Therefore, using the same dimensions intended for the aluminum prototype, but disregarding the thickness, a PVC prototype was constructed and tested on. Figures 15 and 16 show the PVC prototype with the tether attached.

Figure 14: Aluminum Prototype

Figure 15: Components of the PVC Prototype

Figure 16: Complete PVC Prototype Attached to a Styrofoam Monkey Head

Testing

Several tests were conducted on the two prototypes and on the cranial pedestal itself to determine how precisely the design adhered to the original specifications. Important factors included the weight of the device, its ability to protect the microdrive unit, and its ability to be tamper-proof. Hence, the tests carried out involved measurements of weight, physical application of various forces, and qualitative control regarding the ability of the device to prevent the monkey from tampering with it.

WEIGHT OF PROTOTYPE

First, the PVC prototype was weighed, and its weight (0.55 kg) slightly exceeded the maximum weight requirement of 0.5 kg. The aluminum prototype (0.52 kg) also weighed slightly over the requirement; however, this may not be a problem since the aluminum prototype requires further removal of material to provide a custom fit to the monkey's head, thereby reducing its weight. The tether can also provide extra support for the device, so the weight requirement may be flexible. Additionally, there is a possibility of incorporating a pulley system containing a counterweight that attaches to the tether to counterbalance the weight of entire protective device. This would effectively eliminate the current weight limitation.

APPLICATION OF HORIZONTAL FORCES

After the PVC prototype was weighed, it was subjected to various tests of strength and durability. Horizontal forces were applied to the vertical component of the prototype (Figure 17). Forces up to the maximum practical limit of the spring scale (200 N) were applied without failure of the prototype. Thus, the prototype is able to withstand the minimum requirement of 100 N of force. Additionally, the device was unaffected by impacts of considerable strength (which were not quantified). Thus, failure due to impact is unlikely. Due to certain limitations, these tests were not carried out on the aluminum prototype.

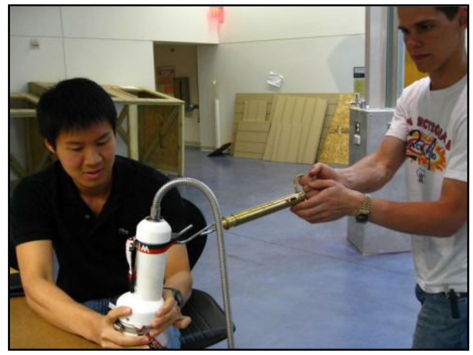

Figure 17: Application of Horizontal Force to PVC Prototype

Having determined the integrity of the device, testing was carried out on the interface where the cranial pedestal meets the skull to determine if failure would occur there before failure of the prototype, resulting in injury to the monkey. A cranial pedestal was implanted into a portion of a monkey skull and secured using dental cement and screws (Figure 18). Horizontal forces were then applied to the cranial pedestal directly. A metal pole was also inserted into the cranial pedestal and horizontal forces were applied to the pole 3 inches above the monkey's skull (Figure 19). In both cases, similar quantitative results to the previous test were obtained. Thus, the monkey's safety would not be compromised since failure at the cranial pedestal is unlikely. The interface was further tested by swinging the pole and impacting the skull into the corner of a table. This caused the skull and dental cement to fracture simultaneously; however, it is unlikely that a monkey would be capable of causing itself harm in such a manner.

Figure 18: Side View of Monkey Skull with Implanted Cranial Pedestal

Figure 19: Application of Horizontal Force to Cranial Pedestal 3 Inches above Monkey's Skull

EASE OF DISASSEMBLY

A final test was administered to determine how easily the monkey could remove the device from its head. To do this, outsiders were asked to attempt to disassemble the PVC prototype as quickly as possible. After several attempts, it was determined that the prototype could not be disassembled without the use of tools. Similarly, it would not be possible for a monkey to disassemble the prototype, especially without the use of tools. Due to certain limitations, the aluminum prototype was not tested for ease of disassembly.

Conclusions

The results from the tests carried out to date indicate that the device meets the design specifications to a large extent. Its weight, while measured at slightly over the maximum requirement, will be further reduced once modifications have been made and the final aluminum prototype completed. Neither the device nor the skull-cranial pedestal interface failed when subjected to forces above those that a monkey could apply (based on the assumption that a monkey would not be able to apply a greater force than a human arm strength estimate of 100 N). Although the aluminum prototype was not tested in this aspect, it is predicted that its strength would be similar to that of the PVC prototype. Further testing must be carried out to assess this claim. Humans were unable to disassemble the device without tools. Assuming that monkeys are less clever and weaker than humans, they would also not be able to disassemble the device without tools. Although only the PVC prototype was tested for ease of disassembly, the aluminum prototype contains similar complexity and intuitively would require tools for disassembly as well. Further testing must be conducted to determine if that is the case.

Future Work

The current aluminum prototype lacks the final cut that is shaped to the contour of the monkey's head to provide a custom fit. The cut was not made because of the lack of an exact mold of the monkey's head, hence accuracy of the cut could not be ensured. Once accurate molds have been obtained, a general shape that will fit all the monkeys will be created and the final cut can then be made. Another component that needs to be completed is the filling of the interior with foam. The foam needs to be molded to the shape of the microdrive unit to provide extra support. The strap system also needs to be improved. Currently, there is only one nylon strap around the chin. Straps that are adjustable to fit all the monkeys used in the research need to be created that go underneath the chin as well as around the neck. This will prevent the monkey from pulling the device off, and will stabilize the device on its head.

Once all these components of the aluminum prototype are completed, further testing must be carried out on it. The tests carried out on the PVC prototype – weight, application of horizontal forces, and ease of disassembly – will be repeated on the aluminum prototype. In addition, a test must be conducted to determine the extent to which the microdrive unit and/or microdialysis probe will be affected by forces applied to the device. In order to do this, forces will be applied to the device and the movement of the microdrive unit and/or microdialysis probe will be measured. This is essential because slight movement of either the microdrive unit and/or microdialysis probe could cause experimental error in data collection or even result in injury to the monkey. After all testing has been completed, the design and prototype will be submitted for approval so that it can be tested on live monkeys.

Other improvements that may be implemented in the future include the addition of a transparent slot in the upper aluminum cylinder so that the microdrive unit can be observed by the researchers during the experiment. This would allow for any disturbances to the microdrive unit to be noticed and corrected. Another possibility to help decrease the amount of weight on the monkey's head is the use of a pulley system connected to the tether. This system would utilize a counterweight to counteract the weight of the device so that it is not felt by the monkey. With this type of setup, weight would become much less of an issue and it may be possible to use a silicone interior as opposed to foam, which would allow for better support. Another issue that needs to be worked out involves the swivel system that attaches to the tether to allow greater freedom for the monkey to turn its head and body. The current swivel was made for blood sampling and the tubing used is too big for the microdialysis tubing used by the researchers. A swivel system that is compatible with this tubing needs to be constructed.

Hopefully once the necessary improvements have been made, the device will be suitable for use by the researchers to improve the microdialysis experimental procedure and create a more comfortable and natural environment for the monkeys.

Ethical Considerations

Since this project involves creating a device for monkeys used in research, there are some ethical issues surrounding the project. Prior to embarking on this project, the team has been assured that all research carried out with these animals follows all governmental regulations and that the animals are treated in a humane manner. There are limitations placed on the amount of experimentation that can be carried out with the monkeys and they are under the constant care of the Wisconsin National Primate Center veterinarians. The goal of this project is to construct a device that ultimately allows the monkeys to be more comfortable and natural while research is being conducted. Hopefully this will improve their quality of life. In addition, when creating the device, the team kept the comfort of the monkey in mind. The team tried to design a device that would be as light and comfortable as possible while still providing the necessary protection. Throughout this process, there has been constant contact with the veterinarians to ensure that the device satisfies all safety requirements and will impact the monkeys in a positive manner.

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APPENDIX I: PRODUCT DESIGN SPECIFICATIONS

PROJECT TITLE:

Development of a Device for Neurochemical Sample Collection from Freely Moving Monkeys
(Project Number: 13 / Project Code: neurochemical_sampling)

INITIAL PROBLEM STATEMENT:

Direct measurements of neurochemical substances in the brain from free moving non-human primates is significantly important for understanding complex brain function and developing treatment strategies for brain disorders in humans. Accordingly, we have modified an existing microdialysis method for application to rhesus monkeys (Frost et al., in press). However, this method requires restraining monkeys in chairs for up to 12 hours while we collect samples. Thus, the purpose of the project is to develop a device allowing monkeys to be free from chairing while experiments are conducted. Although a similar device is available for other studies involved in blood sampling in non-human primates, the development of the device for microdialysis experiments may require creativity and intellectual exercise.

REVISED PROBLEM STATEMENT:

To construct a device that protects the microdialysis apparatus used during cranial experiments on non-human primates. This device will free the monkey from the constraints of chairing while the experiment is conducted and will provide a more comfortable and realistic environment for the monkey. The device should be lightweight, durable, and removable to meet the needs of both the researcher and the subject.

CLIENT REQUIREMENTS:

- Material must be lightweight so as not to impose too much weight on the monkey's head.
- Material must be strong enough to withstand forces that the monkey may apply.
- The device must not interfere with the data collection process.
- The device must be able to be easily integrated with the current microdialysis apparatus being used.
- The monkey must be able to move freely with the device attached to it.
- There should be limited space between the device and the microdialysis apparatus.
- The device must be detachable from the apparatus after use.
- The device should be sterile and reusable.

DESIGN REQUIREMENTS:

1. Physical & Operational Characteristics

a. **Performance Requirements:** The device must be strong enough to withstand 100 N (based on human arm strength estimate) to protect the microdrive unit from any forces that the monkey may apply.

b. **Safety:** The device must not contain sharp edges or other protrusions that may injure the monkey or researcher. The materials that are used must not be toxic.

c. **Accuracy & Reliability:** The device must provide reliable protection for the microdrive unit by being able to withstand a force of 100 N for 10 consecutive hits within a time period of 10 s.

d. **Life in Service:** The device must be able to withstand at least 12 hours of use at a time, and must be sterile so that it can be reused.

e. **Shelf Life:** At least 5 years.

f. **Operating Environment:** Normal laboratory environment for non-human primate research.

g. **Ergonomics:** The device must not restrict the monkey's motion except for the head and neck.

h. **Size:** The base of the device should have a diameter of 3 1/4 in and a maximum height of 2 7/8 in (height differs due to the shaping of the base to provide a custom fit for the Rhesus monkey's head). The upper cylinder should have a diameter of 2 in (with a 1/8 in lip around the bottom) and a height of 6 in.

i. **Weight:** Not more than 0.5 kg so as not to impose too much weight on the monkey's head (as determined by client).

j. **Materials:** Aluminum alloy 5052 for the outer casing and soft foam for the form-fitted interior.

k. **Aesthetics, Appearance & Finish:** The device must be aesthetically pleasing and look "humane" so as not to create a public outcry.

2. Production Characteristics

a. **Quantity:** 1 reproducible device.

b. **Target Product Cost:** Not more than USD1000.

3. Miscellaneous

a. **Standards & Specifications:** The design and construction of the device must comply with USDA regulations and NIH guidelines, subject to approval from the attending veterinarian.

b. **Customers:** Primarily the client, but can be potentially extended to any research institution that is involved with cranial microdialysis studies on non-human primates.

c. **Patient-Related Concerns:** The device must be sterilized before use with a different primate. It should not cause more discomfort to the monkey than the current experimental apparatus (i.e. the primate chair) does.

d. **Competition:** No currently known products specifically address the need to protect the microdrive unit during cranial microdialysis studies on non-human primates.

APPENDIX II: PROJECT EXPENDITURE

SOURCE	ITEM	QUANTITY	TOTAL COST (USD)
The Home Depot	3" × 2' PVC Pipe 2" × 2' PVC Pipe 4"-diameter PVC Pipe Flat Cap 3"-diameter PVC Pipe Cap 2"-diameter PVC Pipe Cap 3" to 2" PVC Pipe Connector 2" to 2" PVC Pipe Connector 3"-diameter PVC Pipe Attachment Great Stuff Big Gap Filler (Foam) Hose Clamps PVC Purple Primer Heavy Duty PVC Cement ¾" × 3' Metal Rod Packet of Screws	1 1 2 1 2 1 1 1 2 4 1 1 1 3	71.75
College Library Printing	Poster	1	35.00
		TOTAL:	**106.75**